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Compilation of Experimental Cancer Therapy Protocol Summaries

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May 1981
Fifth Edition

U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health

Compilation of Experimental Cancer Therapy Protocol Summaries

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U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health

A Service of the
International Cancer Research Data Bank
In Collaboration with the Division of Cancer Treatment

IMPORTANT NOTE

Entries in this compilation are for general informational purposes only. THEY ARE NOT INTENDED TO PROVIDE SUFFICIENT INFORMATION FOR TREATING CANCER PATIENTS.

Many of the therapeutic agents and/or combinations that are used are potentially hazardous and have FDA approval ONLY for clinical treatment investigations by specialists in clinical oncology who are involved in peer-reviewed clinical protocol trials. In some cases, the protocols may not be as effective as existing treatment methods. The reader should contact the group chairman, study chairman, or the principal investigator, who is listed at the beginning of each summary, for further information on a specific protocol.

PREFACE

New procedures, new agents, and new combinations of modalities/agents for treating cancer patients are being tested in more than a thousand experimental clinical trials throughout the world. Collectively these studies cost hundreds of millions of dollars each year.

The *Compilation of Experimental Cancer Therapy Protocol Summaries** was created by the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute (NCI), with the cooperation of the Division of Cancer Treatment, NCI. The purpose of the *Compilation* is to provide a convenient source of information on the nature and scope of clinical trials for investigators and governments around the world.

The fifth edition of the *Compilation* contains summaries of Phase II and Phase III clinical trials currently in progress worldwide. The protocols have been summarized and processed by Informatics Inc. for the ICRDB Program. This edition also includes a brief, preliminary list of several Phase I protocols activated during 1980. This section will be expanded in future editions as investigators provide additional names of new agents used in the Phase I trials.

The basic information in this publication is available for on-line searching on a computer data base called CLINPROT. Detailed information on any of the protocols (including closed protocols) in this publication can be retrieved from the data base by searching a variety of data elements such as tumor type, therapeutic agent, therapy modality, or performing organization.

CLINPROT is updated quarterly and is available through the MEDLARS System of the National Library of Medicine. Information in this data base can be retrieved using computer terminals at over 1,100 locations in the United States, and about 200 locations in 12 other countries.

Readers are encouraged to send comments, suggested changes, or update information on protocols or their status to:

Dr. Hortencia Hornbeak, ICRDB Program
National Cancer Institute
Westwood Building, Room 10A18
Bethesda, Maryland 20205
Phone: (301) 496-7403

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*Previously known as the *Compilation of Cancer Therapy Protocol Summaries*.

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Description of Protocol Summary Elements

Each protocol summary includes the following items:

- Entry number—a five-digit sequential entry number, e.g., 7.0019.
- Title—the phase of the study, type of therapy (including drug names), disease type or site, and, in some cases, the major patient characteristics. Titles may have been edited to include this information.
- Name of the Investigator—the name of the cooperative group chairman, study chairman, or the investigator, followed by his phone number and the name and address of the performing organization.
- Protocol Identification Numbers—the originating group's number, followed, in some cases, by additional identification numbers from other organizations using the same protocol. Protocols received without identification numbers (title only) have been given a number consistent with others in the system.
- Objectives—the major evaluation and comparison goals.
- Protocol Entry Criteria—the specific disease or tumor site under treatment, including any specific limitations for patient entry.
- Protocol Outline—overall treatment scheme.
- Stratification—parameters by which patients are assigned and evaluated.
- Special Study Parameters—nonroutine laboratory and clinical evaluation methods and parameters.
- End Points—those stated in the protocol.
- Current Status—the total number of patients to be entered or the number entered within a specific time period.
- Dosage Schedule—details of treatment, such as dose level, route of drug administration, number of courses, and sequence of drugs or combinations.
- Dosage Forms—the physical form of the drug.
- Date Summarized—the date on which the original protocol was summarized for the computer data base or the date on which significant revision of the summary was made.
- Patient Accrual—an eight-digit number, the four left-hand digits indicating the number of patients and the four right-hand digits indicating the month and year of the accrual.

Explanatory Notes

In this edition of the *Compilation* , the protocols are arranged in seventeen sections as follows:

- Summaries of open protocols for a single, specific type of cancer or tumor site are in the first fourteen sections.
- Summaries of open protocols for unspecified or multiple neoplasms are in Section 15.
- Phase I protocols activated during 1980 are listed in Section 16.
- Protocols known to have been closed during 1980 are listed in Section 17.

All protocols in this publication that are known to have been closed to patient entry during 1980 are listed in Section 17 by title, number, and investigator only. Full summaries of these protocols as well as summaries of protocols closed prior to 1980 will remain in the CLINPROT data base indefinitely.

In addition to the main table of contents, there is a detailed table of contents that precedes each section. Sequential numbers are used to indicate the section and the location within the section of each protocol. For example, protocol 7.0019 is the nineteenth protocol in Section 7. Protocol sequential numbers used in this edition have no relation to those used in earlier editions.

There are three major indexes:

- Tumor Index
- Agent Index
- Protocol Organizational Number Index.

For the purpose of the tumor and agent indexes, surgery and radiotherapy are classified as 'agents'. The cross index of protocol identification numbers is useful in locating identical protocols that are being used by various organizations under different identification numbers.

There are three appendixes:

- Drug names, with their synonyms and acronyms.
- Abbreviations of countries, organizations, and tumor sites that have been used as prefixes in identification numbers of all protocol summaries in CLINPROT.
- Abbreviations of medical and measurement terms used in the summaries.

SUMMARIES OF CANCER THERAPY PROTOCOLS

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EORTC-16802 PHASE II CHEMOTHERAPY WITH ADRIAMYCIN, CARMINOMYCIN AND QUELAMYCIN FOR ADVANCED BREAST CANCER 1.0094

GER-GO-MC-IV/80 PHASE II CHEMOTHERAPY WITH ADR/DAVA FOR METASTATIC BREAST CANCER 1.0095

GER-OSAKO-1177 COMBINATION CHEMOTHERAPY WITH CTX/VCR/ADR AND CTX/MTX/5-FU PLUS IMMUNOTHERAPY WITH C. PARVUM FOR BREAST CANCER 1.0096

ITA-MIL-7802 ADJUVANT CHEMOTHERAPY WITH CMF AND AV COMBINATIONS, DBD, HMM, MITO AND HORMONE THERAPY WITH TMX/MPA FOR BREAST CANCER IN PREMENOPAUSAL WOMEN 1.0097

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UICC-73047 CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE ADJUVANT TO RADICAL MASTECTOMY FOR PRIMARY OPERABLE BREAST CARCINOMA 1.0100

UICC-76026 ADJUVANT CHEMOTHERAPY WITH L-PAM VS CTX/MTX/5-FU FOR OPERABLE CARCINOMA OF THE BREAST 1.0101

UICC-76116 HORMONE THERAPY WITH MEDROXYPROGESTERONE ACETATE VS OOPHORECTOMY FOR ADVANCED METASTATIC OR INOPERABLE BREAST CARCINOMA 1.0102

UKM-KCH-BR3 ADJUVANT CHEMOTHERAPY WITH CTX AND ANTIESTROGEN THERAPY WITH TMX, ALONE OR COMBINED, FOR BREAST CARCINOMA 1.0103

UKM-RI-B-1 COMPARATIVE STUDY OF SURGERY/RADIOTHERAPY WITH OR WITHOUT RICH REGIMEN FOR CARCINOMA OF THE BREAST 1.0104

UKM-RMH-BR-1A ADJUVANT AMINOGLUTETHIMIDE PLUS HYDROCORTISONE FOR POOR-RISK PRIMARY STAGE II BREAST CANCER 1.0105

UKM-RMH-BR-1B ANTIHORMONAL THERAPY WITH AMINOGLUTETHIMIDE VS TAMOXIFEN FOR ADVANCED METASTATIC BREAST CANCER 1.0106

SECTION 1

BREAST TUMORS

1.0001 PHASE III CHEMOTHERAPY WITH CAFVP (CTX/ADR/5-FU/VCR/PRED) PLUS SURGERY OR RADIOTHERAPY FOR STAGE III BREAST CARCINOMA

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-7784

OBJECTIVES:

I. Test the relative efficacy of surgery versus radiotherapy when either is performed following chemotherapy and prior to subsequent chemotherapy with CAFVP.

II. Determine patterns of relapse sites following mastectomy or radiotherapy. Evaluate patient tolerance to the two regimens, and investigate the relationship of estrogen receptor status to therapeutic outcome.

III. Evaluate immunologic parameters (quantitative T- and B-cell analysis, phytohemagglutinin and pokeweed mitogen stimulation) and correlate these with clinical parameters.

IV. Carry out serial evaluation of patient's psychosocial status.

V. Test the effectiveness of CAFVP in converting inoperable cases to operable ones.

PROTOCOL ENTRY CRITERIA: Patients less than 75 years old with histologically diagnosed and clinically staged breast carcinoma. Patients must have Stage III disease, no distant metastases, nor malignant mammary tumors other than carcinoma, no other primary malignant neoplasm other than basal cell or squamous cell carcinoma of the skin or carcinoma in situ of the cervix. Patients must have adequate renal, liver, and hematological function and have received no prior treatment for breast tumors.

PROTOCOL OUTLINE: Randomized study, except for initial Chemotherapy. Enter all patients to Regimen A.

Regimen A: 4-Drug Combination Chemotherapy plus Hormone Therapy. CAFVP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Re-evaluate for operability and no evidence of metastases. Remove from study patients who develop progressive disease during initial Chemotherapy. Randomize all others to Arm I or Arm II.

Arm I: Surgery plus 4-Drug Combination Chemotherapy plus Hormone Therapy. Modified radical or radical mastectomy plus CAFVP, with substitution of ADR when maximum dose is reached, by Methotrexate, MTX, NSC-740.

Arm II: Radiotherapy plus 4-Drug Combination Chemotherapy plus Hormone Therapy. Megavoltage radiation plus CAFVP.

STRATIFICATION BY: Site of primary tumor, size of primary tumor, participating institutions.

SPECIAL STUDY PARAMETERS: Bone scan, bone survey, estrogen receptor assay, psychosocial assessment, skin testing for recall antigens.

END POINTS: Response/remission rate, recurrence rate, toxicity/morbidity of treatment, disease-free interval.

CURRENT STATUS: 235 patients will be entered in 4 years.

DOSAGE SCHEDULE:

Regimen A: CAFVP given q 28 days for 3 courses. CTX - 100 mg/sqm/day po on days 1 through 14; ADR - 25 mg/sqm iv on days 1 and 8; 5-FU - 500 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm iv on days 1 and 8 (maximum single dose 2 mg); PRED - 40 mg/sqm po on days 1 through 14.

Evaluate all patients within 2 to 6 weeks after completion of Regimen A. Remove patients with nonresectable or metastatic disease from study. Randomize those patients that qualify for Surgery to Arm I or Arm II. Separately randomize patients with T3a or T3b vs. patients with T4a, T4b, or T4c disease. (Patients not qualifying for Surgery nonrandomly receive Radiotherapy (Arm II); if neither Surgery nor Radiotherapy can be administered, patients are removed from study. Addendum 1, June 1980.)

Arm I: Perform Surgery within 2 to 6 weeks of completion of prior therapy. Upon wound healing, and 2-6 weeks following the Surgery, resume Chemotherapy with CAFVP, as in Regimen A. When the maximum cumulative ADR dose of 550 mg/sqm is reached, substitute MTX - 40 mg/sqm (30 mg/sqm for patients over 60 years of age) iv on days 1 and 8 of each monthly course. Continue Chemotherapy for 2 years or until relapse.

Arm II: Radiotherapy: To 2 tangential breast fields, plus 'hockey-stick' field encompassing the axillary, internal mammary, and supraclavicular lymphnode areas - 5000 rad given in 5 weeks, plus 1500 to 2000 rad boost given in 2 weeks to the axillary nodes. Resume Chemotherapy with CAFVP within 2 to 6 weeks - as in Arm I.

For CNS metastases, irradiate whole brain through two lateral parallel opposed fields - 4200 rad midplane dose for 2 weeks while continuing Chemotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 50 mg tablets; MTX - 50 mg vials; 5-FU - 500 mg vials; VCR - 1 and 5 mg vials; ADR - 10 and 50 mg vials; PRED - 5 and 50 mg tablets.

DATE SUMMARIZED: 05/79

1.0002 PHASE II CHEMOTHERAPY WITH SPIROGERMANIUM FOR RECURRENT OR REFRACTORY ADENOCARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) CLB-8076

OBJECTIVES:

I. Evaluate, in a Phase II study, the presence or absence of antitumor activity of spirogermanium in the treatment of inoperable, advanced, or recurrent adenocarcinoma of the breast.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented, clearly measurable, inoperable or recurrent adenocarcinoma of the breast who are not eligible for a higher priority CALGB study. Patients must have failed on standard chemotherapy (minimum of 4 weeks of treatment) and must have received no more than two prior chemotherapeutic programs. Patients must have an expected survival of at least 2 months, and hematologic, renal, and hepatic functions must be adequate. The CALGB performance score must be 3 or less. A minimum of 4 weeks must have elapsed from the time of prior chemotherapy, radiotherapy, or palliative surgery (2 weeks if progressive disease is present).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Spirogermanium, NSC-192965.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic, renal, and hepatic function tests; chest x-ray; serum glucose; calcium/uric acid.

END POINTS: Response/remission rate, duration of response, duration of survival, clinical toxicity of treatment.

CURRENT STATUS: Initially, 20 patients will be entered. If there is at least one response among the first 20 patients, at least 40 patients will be required.

DOSAGE SCHEDULE:

Spirogermanium - 80 mg/sqm iv infusion over no less than 60 minutes. The drug is given every other day (Mon., Wed., and Fri.) for 2 weeks, then 2 times a week (Mon. and Thurs.) for 2 weeks; thereafter, it is given once a week. Treatment is continued until there is evidence of objective progression of disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Spirogermanium - 10 mg vials.

DATE SUMMARIZED: 12/80

1.0003 PHASE III CHEMOTHERAPY WITH CTX/ADR/5-FU/MTX WITH OR WITHOUT TMX HORMONE THERAPY FOR ADVANCED POSTMENOPAUSE BREAST CARCINOMA

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PROTOCOL NUMBER(S) CLB-8081

OBJECTIVES:

I. Compare cyclophosphamide (CTX)/adriamycin (ADR)/5-fluorouracil (5-FU)/methotrexate (MTX) to CTX/ADR/5-FU/MTX plus tamoxifen (TMX) in postmenopausal women with advanced breast cancer.

II. Determine if estrogen receptor status is prognostic of response to chemotherapy.

PROTOCOL ENTRY CRITERIA: Pre- (Addendum 1, April 1980) and postmenopausal patients with measurable, histologically confirmed metastatic, locally recurrent or surgically incurable carcinoma of the breast. Patients must be 75 years of age or less with a CALGB performance status of 3 or less and adequate hematologic, renal and hepatic status.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893; plus Tamoxifen, TMX, NSC-180973. Requires substitution of Methotrexate, MTX, NSC-740 for ADR after maximum dose of ADR is reached.

Arm II: 3-Drug Combination Chemotherapy. CTX; ADR; 5-FU. MTX substitution as in Arm I.

STRATIFICATION BY: Participating institutions; estrogen receptor status: positive vs. negative vs. unknown; dominant disease site: visceral vs. soft tissue or osseous; prior therapy: yes vs. no. (Premenopausal women will be randomized within a single stratum. Addendum 1, April 1980.)

SPECIAL STUDY PARAMETERS: Estrogen receptor assay; bone, liver and brain scans; skin tests.

END POINTS: Response/remission rate, objective tumor response, duration of response, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: Approximately 280 patients to be entered in 24 months.

DOSAGE SCHEDULE:

Arm I: CTX - 100 mg/sqm po on days 1 through 14; ADR - 25 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on days 1 and 8; 5-FU - 500 mg/sqm iv on days 1 and 8 plus TMX - 20 mg po daily. Repeat q 28 days. Replace ADR when maximum dose is reached with MTX. Continue until disease progression.

Arm II: CTX, ADR, 5-FU, MTX as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 25 and 50 mg tablets; ADR - 10 and 50 mg vials; 5-FU - 500 mg ampules; MTX - 2.5 and 25 mg vials; TMX - 10 mg tablets.

DATE SUMMARIZED: 06/80

1.0004 TWO CMFVP (CTX/MTX/5-FU/VCR/PRED) REGIMENS WITH OR WITHOUT VATH (VBL/ADR/THIOTEPA/FXM) AS ADJUVANT CHEMOTHERAPY FOR BREAST CANCER

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PROTOCOL NUMBER(S) CLB-8082

OBJECTIVES:

I. Compare the relative efficacy of 2 different schedules of CMFVP (cyclophosphamide/methotrexate/5-fluorouracil/vincristine/prednisone) Maintenance chemotherapy after conventional CMFVP Induction in patients who have undergone mastectomy for breast cancer.

II. Compare the relative efficacy of VATH (vinblastine/adriamycin/thiotepa/halotestin) given at increasing doses vs. continuation of CMFVP chemotherapy in prolonging the disease-free interval.

III. Evaluate patient tolerance to each of these therapeutic regimens and the percent of 'ideal' total drug actually administered.

IV. Determine the relationship between axillary node status at the time of mastectomy and disease-free interval with each of the drug regimens.

V. Analyze the relationship between menopausal status and each of the four regimens of multi-drug intensive chemotherapy in terms of prolonging the disease-free interval.

VI. Determine the effect of estrogen receptor protein status on chemotherapeutic response.

VII. Determine the effect of the four different adjuvant chemotherapy regimens on the site of recurrence.

PROTOCOL ENTRY CRITERIA: Post-mastectomy breast cancer patients not over the age of 75 years in whom the tumor was clinically confined to the breast or breast and axilla. The tumor must have been nonulcerating and movable in relation to the fascia and/or chest wall. Palpable axillary nodes must also have been movable. Surgery must have consisted of a conventional or modified radical mastectomy with removal of the breast and at least the lower axillary contents, preferably by en bloc resection. Pathologic finding of metastatic disease in one or more axillary lymph nodes must be documented. There may be no distant metastases. Patients may not have received prior radiotherapy, chemotherapy, or hormonal therapy for breast cancer or any surgery other than that specified. Bone marrow and renal function must be normal. The breast cancer must be unilateral and there may be no previous or concomitant cancer except squamous or basal cell carcinoma of the skin, carcinoma in situ of the cervix curatively treated, or lobular carcinoma in situ found by mirror-image biopsy at the time of primary surgery. No more than 8 weeks may have intervened between mastectomy and the time of entry.

PROTOCOL OUTLINE: Randomized study. Enter all patients to Regimen A. Then randomize patients to Arms I or Arm II. Then rerandomize patients in Arm I to Arms III or IV and those in Arm II to Arms V or VI.

Induction.

Regimen A: 4-Drug Combination Chemotherapy plus Hormone Therapy. CMFVP: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; Vincristine, VCR, NSC-67574; plus Prednisone, PRED, NSC-10023.

Maintenance.

Arm I: 4-Drug Combination Chemotherapy plus Hormone Therapy. CMFVP on conventional 28-day cycles.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy. CMFVP in 6-week courses.

Arm III: 4-Drug Combination Chemotherapy plus Hormone Therapy. CMFVP as in Arm I.

Arm IV: 3-Drug Combination Chemotherapy plus Hormone Therapy. VATH: Vinblastine, VBL, NSC-49892; Adriamycin, ADR, NSC-123127; Thiotepa, NSC-6396; plus Halotestin, Fluoxymesterone, FXM, NSC-12165.

Arm V: 4-Drug Combination Chemotherapy plus Hormone Therapy. CMFVP as in Arm III.

Arm VI: 3-Drug Combination Chemotherapy plus Hormone Therapy. VATH as in Arm IV.

STRATIFICATION BY: Menopausal status (pre vs. post), number of positive axillary nodes (1-3 vs. 4-9 vs. more than 10).

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-12, liver function tests, chest x-ray, bone scan, liver scan, estrogen receptor status, psychosocial evaluation.

END POINTS: Disease-free interval, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 850 patients will be required.

DOSAGE SCHEDULE:

Regimen A: CTX - 80 mg/sqm po daily in divided doses for 42 days; MTX - 40 mg/sqm/week iv for 6 weeks (30 mg/sqm in patients aged 60 years and over); 5-FU - 500 mg/sqm/week iv for 6 weeks; VCR - 1.0 mg/sqm/week (maximum 1.5 mg) for 6 weeks; PRED - 40 mg/sqm/day po in 3 divided doses for 21 days, then tapered to zero over 6 days. 5-FU is to be followed by VCR followed by MTX. Treatment should begin as soon after Surgery as wound healing permits, preferably within 2-4 weeks.

Arm I: CMFVP: CTX - 100 mg/sqm/day po in divided doses on days 1 through 14; MTX - 40 mg/sqm (30 mg/sqm in patients 60 years or older) iv on days 1 and 8; 5-FU - 500 mg/sqm iv on days 1 and 8; VCR - 1.0 mg/sqm (maximum 1.5 mg) on days 1 and 8; PRED - 40 mg/sqm/day po in 3 divided doses on days 1 through 14 without tapering. Begin treatment following 2 weeks rest after Regimen A. Repeat at 28-day intervals for a total of 6 courses.

Arm II: CMFVP: Identical drugs and dosages as in Regimen A. Begin treatment after a rest period of 6 weeks following Regimen A and give a total of 3 courses separated by 6-week rest periods.

Arm III: CMFVP: Identical to treatment in Arm I. Give six 28-day cycles.

Arm IV: VATH: VBL - 1.5 mg/sqm iv on days 1 and 29; ADR - 15 mg/sqm iv on days 1 and 29; Thiotepa - 4 mg/sqm iv on days 1 and 29; FXM - 30 mg/day po in 3 divided doses. Begin treatment 2 weeks after completion of the last course of treatment in Arm I. In the absence of prohibitive toxicity, give 2 more courses of VATH with VBL, ADR, and Thiotepa, at twice the dosage as in the first course for the second course and at three times the dosage for the third course. FXM is given at the same dosage for all three courses.

Arm V: CMFVP: Two additional courses as in Arm II.

Arm VI: VATH: Two additional courses as in Arm IV.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 25 and 50 mg tablets; MTX - 5 and 50 mg vials; 5-FU - 500 mg vials; VCR - 1 and 5 mg vials; PRED - 5, 10, 20, and 50 mg tablets; VBL - 10 mg vials; ADR - 10 and 50 mg vials; Thiotepa - 15 mg vials; FXM - 5 and 10 mg tablets.

DATE SUMMARIZED: 12/80

1.0005 PHASE II PILOT CHEMOTHERAPY WITH PALA FOR RESISTANT METASTATIC ADENOCARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) EST-PA-179

OBJECTIVES:

I. Determine the ability of PALA to cause tumor shrinkage or stabilization of breast cancer which has proven to be resistant to conventional drug therapy.

II. Assess the toxicity of PALA in patients with prior chemotherapy exposure.

PROTOCOL ENTRY CRITERIA: Patients under 70 days of age with histologically proven measurable (or evaluable, Addendum 2, February 1980) metastatic breast adenocarcinoma resistant to conventional systemic therapy. Patients must have a performance status of 2 or better, and must have adequate hematologic, renal and hepatic functions. Three weeks must have elapsed since prior chemotherapy (which must not have included study drug) and since prior surgical hormonomanipulation which must have been followed by documented disease progression. Progressive disease must also have been demonstrated within 12 weeks of initiation of any prior medical hormonomanipulation, without improvement within 7 days of withdrawal of such therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION: Not given.

SPECIAL STUDY PARAMETERS: Bone and liver scans, liver and kidney function tests.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment survival.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

PALA - 1,500 mg/sqm/day iv 20 min infusion on days 1 through 5 q 3 weeks. Continue therapy for at least 1 month and until evidence of disease progression. Treat brain metastases with whole brain radiotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 10 ml ampules.

DATE SUMMARIZED: 12/79

1.0006 PILOT COMBINATION CHEMOTHERAPY WITH HIGH-DOSE CMFP (CTX/MTX/5-FU/PRED) FOR RECURRENT AND/OR METASTATIC BREAST CARCINOMA

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PROTOCOL NUMBER(S) EST-PA-180

OBJECTIVES:

I. Determine the toxicity of high-dose CMFP: cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU)/prednisone (PRED).

II. Determine the effectiveness of high-dose CMFP in achieving responses in patients who have recurrent breast carcinoma following CMF, CMFP, or CMFP plus tamoxifen adjuvant chemotherapy.

III. Determine the effectiveness of high-dose CMFP in achieving increased complete responses and longer duration of responses in patients with metastatic breast carcinoma who have not received prior chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients 50 years of age or less with histologically documented diagnosis of breast carcinoma with recurrent and/or metastatic disease that is measurable or evaluable. The performance status (ECOG) must be 0, 1, or 2. WBC and platelet counts and hepatic and renal functions must be adequate. There must be no prior chemotherapy other than CMF, CMFP or CMFP plus tamoxifen given as adjuvant therapy, and this therapy must have been discontinued at least 6 months prior to entry. Prior radiotherapy for breast carcinoma is acceptable if limited and not inclusive of 50 percent of the pelvic bone structure and lower spine. There must be no history of malignant neoplasms aside from curatively treated basal or squamous cell carcinoma of the skin or cured cervical carcinoma.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. CMFP: Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740, with Citrovorum Factor, CF, NSC-3590; plus Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Bone survey, bone scan, liver and brain scan, CEA, bone marrow aspiration and biopsy, EKG.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

Induction:

CMFP (high-dose): CTX - 1000 mg/sqm iv on days 1 and 8; MTX - 3 g/sqm iv infusion over 1 hour on days 1 and 8, followed in 24 hours by Citrovorum Factor - 10 mg/sqm po q 6 hours for 12 doses; 5-FU - 900 mg/sqm iv infusion over 1 hour given 1 hour after completion of MTX infusion on days 1 and 8; plus PRED - 40 mg/sqm po on days 1 through 14. After completion of 1 cycle, patients with stable or progressive disease will be taken off study; CR or PR patients will receive 2nd cycle of high-dose therapy, beginning 28 days after the 1st cycle. Patients will then be evaluated again; CR and PR patients will go to Maintenance, and patients showing no change or progression will be taken off study.

Maintenance:

CMFP (standard dose): CTX - 100 mg/sqm po on days 1 through 14; MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8; plus PRED - 40 mg/sqm po on days 1 through 14. Repeat q 28 days. Patients showing CR or PR continue therapy until progression, at which time they will be taken off study; patients showing no change will also be taken off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 1 g vials; CTX - 200 and 500 mg vials; 5-FU - 500 mg vials; PRED - 5, 10 and 20 mg tablets.

DATE SUMMARIZED: 10/80

1.0007 PILOT STUDY CHEMOTHERAPY AND HORMONE THERAPY WITH CMFP (CTX/MTX/5-FU/PRED) FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) EST-PB-179

OBJECTIVES:

I. Determine effects of CMFP: cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU)/prednisone (PRED) on metastatic breast cancer.

PROTOCOL ENTRY CRITERIA: Adult women with measurable, metastatic breast cancer who have had no prior chemotherapy. Patients must have adequate kidney function and must not have hormonal therapy in prior month.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. CMFP: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; plus Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurement; ECOG performance scale; CBC; kidney, liver, and bone function; bone and liver scan; bone marrow; skeletal survey.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 20 patients will be entered in 6 months.

DOSAGE SCHEDULE:

CMFP: CTX - 100 mg/sqm po on days 1 through 14 at bedtime; MTX - 200 mg/sqm iv on days 1 and 8 before CTX; 5-FU - 600 mg/sqm iv 1 hour after the end of MTX; PRED - 40 mg/sqm po on days 1 through 14 at bedtime; Leukovorin - 10 mg/sqm po q 6 hours for 6 doses beginning 24 hours after MTX. Repeat q 28 days. Continue treatment until disease progression. In event of a 6-month complete remission, continue treatment for 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 20 and 50 mg tablets; MTX - 50 mg vials; 5-FU - 500 mg ampules; PRED - 5, 20, and 50 mg tablets.

DATE SUMMARIZED: 02/80

1.0008 CONSOLIDATION HEMI-BODY IRRADIATION WITH CHEMOTHERAPY WITH CMFP (CTX/MTX/5-FU/PRED) OR CAF (CTX/ADR/5-FU) FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) EST-PE-179

OBJECTIVES:

I. Examine the effect of hemi-body irradiation (upper and lower halves) in patients who have achieved PR or CR with 6 cycles of CMFP (cyclophosphamide, methotrexate, 5-fluorouracil, prednisone) or CAF (cyclophosphamide, adriamycin, 5-fluorouracil).

II. Determine whether the addition of 600 rad half-body irradiation and supplemental irradiation to bulky and/or symptomatic tumor areas can maintain, increase, or prolong remissions obtained by chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with recurrent or metastatic breast cancer with histologically documented primary breast cancer in PR or CR by ECOG criteria. Patients must be no older than 70 years, have a performance status of 3 or better, and have adequate hematological parameters and evidence of adequate renal and hepatic function. Patients may not have had prior breast irradiation prophylactically or for local recurrence.

PROTOCOL OUTLINE: Nonrandomized study. Patients may receive either Regimen A or Regimen B; responders from both enter Regimens C and D.

Regimen A: 3-Drug Combination Chemotherapy plus Hormone Therapy. CMFP: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; Prednisone, PRED, NSC-10023.

Regimen B: 3-Drug Combination Chemotherapy. CAF: CTX; Adriamycin, ADR, NSC-123127; 5-FU.

Regimen C: Radiotherapy. Upper and lower half-body irradiation from a source of at least 1 MeV.

Regimen D: 3-Drug Combination Chemotherapy. CMF: CTX; MTX; 5-FU.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurement, hematological parameters, liver function tests, EKG, chest x-ray, bone and liver scans, skeletal survey.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Twenty evaluable patients will be entered.

DOSAGE SCHEDULE:

Regimen A: CMFP: CTX - 100 mg/sqm/day po on days 1 to 14; MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8; PRED - 40 mg/sqm po on days 1 to 14. Repeat q 4 weeks for a maximum of 6 months.

Regimen B: CAF: CTX - 100 mg/sqm/day on days 1 to 14; ADR - 30 mg/sqm iv on days 1 and 8; 5-FU - 500 mg/sqm iv on days 1 and 8. Repeat q 4 weeks for a maximum of 6 weeks.

Enter all PR and CR from Regimens A and B to Regimens C and D.

Regimen C: Megavoltage irradiation with 600 rads at 30-40 rads/min to the upper half of the body followed in 6 weeks by 600 rads to the lower half of the body. Supplemental irradiation for symptomatic or bulky disease may also be indicated.

Regimen D: Start 1 month following Regimen C Radiotherapy. CMF: CTX, 5-FU, MTX - all as in Regimen A.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 25 and 50 mg tablets; 5-FU - 500 mg vials; MTX - 50 mg vials; PRED - 5, 20, and 50 mg tablets.

DATE SUMMARIZED: 07/80

1.0009 PILOT STUDY CHEMOTHERAPY WITH ADR PLUS AMSA FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) EST-PF-179

OBJECTIVES:

I. Ascertain the toxicity and determine the optimum dosages of a combination of adriamycin and m-AMSA.

II. Make a preliminary estimate of the efficacy of adriamycin combined with m-AMSA in patients with metastatic breast cancer who have failed on prior chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented breast cancer who have recurrent and/or metastatic disease and who have evidence of progressive disease with measurable or evaluable disease as defined by standard ECOG criteria. Patients must have prior exposure to at least one chemotherapy program, although they may not have been treated with adriamycin or m-AMSA. Patients must be under 70 years old and must be ineligible for hormonal treatment. The performance status must be 3 or 4, the hematological parameters must be adequate, and there must be evidence of adequate renal and hepatic function. Patients may not have congestive heart failure, significant arrhythmia, or myocardial infarction in the previous 6 months.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurement, chest x-ray, ejection fraction, EKG, hematologic parameters, kidney and liver function tests, bone scan or survey, liver scan.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: About 60 patients will be entered.

DOSAGE SCHEDULE:

ADR - 40 mg/sqm iv bolus q 3 weeks, maximum cumulative dose not to exceed 500 mg/sqm; AMSA - 50 mg/sqm iv over 30 minutes q 3 weeks. Dose of AMSA to be increased by increments of 20 mg/sqm for each group of 5 patients. Doses higher than 50 mg/sqm are to be administered over 60 minutes.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 5 and 50 mg vials; AMSA - 75 mg ampules.

DATE SUMMARIZED: 07/80

1.0010 LONG-TERM MAINTENANCE WITH CURRENT THERAPY FOR PATIENTS IN COMPLETE REMISSION FROM METASTATIC BREAST CARCINOMA

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PROTOCOL NUMBER(S) EST-1177

OBJECTIVES:

I. Compare the response durations and survival obtained with vs. without continued maintenance therapy to assess the desirability of continuing therapy in patients with metastatic breast cancer in complete remission at two years.

II. Assess the prognostic importance of drug regimens, age, and pretreatment variables of performance status, dominant disease, disease-free interval, etc., for their impact upon response duration and survival.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented diagnosis of metastatic mammary carcinoma which has recurred locally and/or distally and been under treatment with systemic chemotherapy and/or chemohormonotherapy for at least 2 years, but not more than 30 months. Patients must have undergone 2 complete remissions six months apart, and must be in complete remission for 6 months or more.

PROTOCOL OUTLINE: Randomized study.

Arm I: Continue current therapy until relapse.

Arm II: Discontinue all current treatment except replacement therapy for prior adrenalectomy. Observe patients. Reinstate prior therapy upon recurrence. Remove from study patients with objective relapse.

STRATIFICATION BY: Age: over vs. under 52; current therapy: single-agent chemotherapy with or without hormone therapy vs. ECOG combination chemotherapy vs. non-ECOG combination chemotherapy; duration of complete remission: 6 to less than 12 months vs. 12 months or longer.

SPECIAL STUDY PARAMETERS: Skin tests; liver, bone and brain scans; tomography of suspicious areas.

END POINTS: Response duration, survival.

CURRENT STATUS: 65 to 70 patients will be entered.

DOSAGE SCHEDULE: Not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/78

PATIENT ACCRUAL: 00110978

1.0011 ADJUVANT THERAPY WITH TAMOXIFEN FOR OLDER POSTMENOPAUSAL PATIENTS WITH STAGE II BREAST CANCER

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1178

OBJECTIVES:

I. Compare effect of adjuvant hormonal therapy with tamoxifen for postmenopausal patients over 65 years of age to placebo control group.

II. Assess importance of estrogen receptor status on course of disease and on influence of hormone therapy.

PROTOCOL ENTRY CRITERIA: Patients over 65 years of age with radical or modified radical mastectomy for potentially curable noninflammatory breast carcinoma who have one or more histologically-proven tumor positive axillary nodes. Patients must have a movable tumor confined to one breast and the ipsilateral axilla, adequate hematologic, renal and hepatic function, and normal bone scan (unless abnormality is due to nonmalignant cause). Patients must be free of: malignant breast tumors other than carcinoma, prior therapy for any kind for breast cancer, preoperative ulceration or infiltration of skin larger than 2 cm greatest diameter or peau d'orange involving more than 1/3 the breast, satellite or parasternal nodules, edema of the arm, 'superradical' mastectomy, ipsilateral involved axillary node(s) that are fixed or larger than 2 cm greatest diameter, and any metastases other than prescribed axillary nodes.

PROTOCOL OUTLINE: Randomized study. Enter patients within 2 to 10 weeks of mastectomy.

Arm I: Placebo.

Arm II: Single-agent Hormone Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions; lymph node status: 1 to 3 positive vs. 4 or more positive; estrogen receptor status: positive vs. indeterminate vs. unknown.

SPECIAL STUDY PARAMETERS: Bone scan, xeromammogram or mammogram, estrogen receptor status.

END POINTS: Objective tumor response, length of survival, disease free interval, toxicity/morbidity of treatment, recurrence rate, survival time, survival rate.

CURRENT STATUS: About 166 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Begin treatment between 2 and 10 weeks after mastectomy.

Arm I: Placebo - twice a day po for 24 months.

Arm II: TMX - 20 mg/day in 2 divided doses po for 24 months.

Remove from study patients with evidence of treatment failure. Follow patients for life.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - 10 mg tablets.

DATE SUMMARIZED: 10/78

1.0012 PHASE III CHEMOTHERAPY WITH ADR/DBD/TMX VS MITO/TMX VS MITO/TMX/FXM AFTER PRIOR SYSTEMIC THERAPY FOR METASTATIC BREAST CANCER

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1179

OBJECTIVES:

I. Compare in patients with metastastic or recurrent mammary carcinoma the effects of adriamycin (ADR)/dibromodulcitol (DBD)/tamoxifen (TMX) vs. mitomycin C (MITO)/TMX in patients without previous ADR (or DBD, Addendum 1, May 1979) exposure, and MITO/TMX vs. MITO/TMX/fluoxymesterone (FXM) in patients with prior ADR (and/or DBD, Addendum 1, May 1979) exposure.

II. Determine the effect of FXM on drug dosage and cumulative toxicity of MITO/TMX.

III. Evaluate retrospectively the effect of prior chemotherapy on response and toxicity.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable or evaluable, recurrent or metastatic progressive mammary carcinoma who have had prior exposure to at least one chemotherapy program that did not include MITO, DBD, or TMX. (Patients with prior exposure to ADR and/or DBD are eligible. Addendum 1, May 1979.) Patients with prior exposure to FXM are eligible only if they have not received ADR (or DBD, Addendum 1, May 1979). Patients must have an ECOG performance rating of at least 3, adequate hematologic function, and normal liver and kidney function. Patients must not be eligible for a higher priority protocol. Patients with prior surgical-hormonal therapy must have undergone surgery at least 3 weeks ago and have confirmed disease progression. Patients with prior chemo-hormonal therapy must have progressive disease within 12 weeks of initiating therapy and no improvement within 7 days after withdrawal of the therapy, or they must, after relapsing and being withdrawn from therapy, show documented, further progressive disease over at least 10 days off hormonal therapy.

PROTOCOL OUTLINE: Randomized study. Randomize patients with no prior ADR and DBD exposure to Arms I or II. Randomize patients with prior ADR and/or DBD exposure to Arms II or III. (Randomization with respect to DBD per Addendum 1, May 1979.)

Arm I: 2-Drug Combination Chemotherapy plus Hormone Therapy. Adriamycin, ADR, NSC-123127; Dibromodulcitol, DBD, NSC-104800; Tamoxifen, TMX, NSC-180973.

Arm II: Single-agent Chemotherapy plus Hormone Therapy. Mitomycin-C, MITO, NSC-26980; TMX.

Arm III: Single-agent Chemotherapy plus 2-Drug Hormone Therapy. MITO; TMX; Fluoxymesterone, FXM; NSC-12165

STRATIFICATION: Participating institutions; prior drug exposure; prior ADR and/or DBD without FXM vs. no prior ADR and/or DBD with FXM vs. no prior ADR, DBD or FXM; disease site: dire visceral vs. all other; response to prior hormone therapy: response vs. no response vs. no prior hormone therapy; estrogen receptor status: positive vs. negative vs. unknown; ECOG performance: 0 or 1 vs. 2 or 3. (Stratification with respect to DBD per Addendum 1, May 1979)

SPECIAL STUDY PARAMETERS: Liver, kidney, and bone marrow function tests; CEA; EKG; bone survey; bone, liver, brain and CT scans; ER assay.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival time.

CURRENT STATUS: 260 patients will be entered in 2.5 years.

DOSAGE SCHEDULE:

Arm I: ADR - 40 mg/sqm (maximum total dose 475 mg/sqm) iv on day 1; DBD - 135 mg/sqm po on days 2 through 11; TMX - 20 mg/day po. Repeat course q 28 days. When maximum dose of ADR is reached, substitute MITO - 5 mg/sqm iv q 35 days.

Arm II: MITO - 12 mg/sqm iv on day 1; TMX - 20 mg/day po. Repeat course q 35 days.

Arm III: MITO - 12 mg/sqm iv on day 1; TMX - 20 mg/day po; FXM - 20 mg/day po. Repeat course q 35 days.

Continue therapy until disease progression. Remove from study patients with progressive disease after 1 course, no change after 2 courses if associated with an increase of 2 points in analgesia requirements or a decrease of 1 in ECOG performance status, no change after 3 courses if associated with a subjective feeling of no change manifested by an analgesia requirement of 2 or more or a decrease of 2 or more in performance status, or complete remission at 2 years permitting entry into Maintenance phase of Protocol EST-1177.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; DBD - 50 and 100 mg tablets; MITO - 5 mg vials; FXM - 5 mg tablets; TMX - 10 mg tablets.

DATE SUMMARIZED: 04/80

1.0013 PHASE II CHEMOTHERAPY WITH ADR/VCR, ADR/VCR/DBD, ADR/VCR/ICRF-159, OR DBD ALONE FOR DISSEMINATED BREAST CARCINOMA

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PROTOCOL NUMBER(S) EST-2175; UICC-76064

OBJECTIVES:

I. Evaluate and compare the anti-tumor activities of 3 combination chemotherapy regimens: adriamycin (ADR) and vincristine (VCR) alone, ADR and VCR plus dibromodulcitol (DBD), and ADR, VCR and ICRF-159.

II. Determine whether the addition of DBD or ICRF-159 to ADR plus VCR therapy can prolong the effective treatment period.

PROTOCOL ENTRY CRITERIA: Patients less than 70 years of age with measurable lesions of recurrent or metastatic breast cancer. Patients must not be eligible for a higher priority protocol and must have performance status no greater than 3.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I, II and III. When total permissible ADR has been given, enter partial and complete responders to Arm IV.

Arm I: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574.

Arm II: 3-Drug Combination Chemotherapy. ADR, VCR plus Dibromodulcitol, DBD, NSC-104800.

Arm III: 3-Drug Combination Chemotherapy. ADR, VCR plus ICRF-159, NSC-129943. (Arm discontinued, Addendum 2, March 1978).

Arm IV: Single-agent Chemotherapy. DBD.

STRATIFICATION BY: Participating institutions, performance status: 0 or 1 vs. 2 and 3; dominant metastatic sites: visceral vs. osseous vs. local or soft tissue.

SPECIAL STUDY PARAMETERS: Bone, liver and brain scans; skin tests: PPD intermediate, mumps, Candida, Varidase.

END POINTS: Response/remission rate, duration of response, length of survival, survival rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: ADR - 60 mg/sqm (maximum cumulative dose - 500 mg/sqm Addendum 1, February 1976) iv on day 1; VCR - 1.2 mg/sqm (maximum single dose - 2 mg) iv on day 1. Repeat course q 3 weeks.

Arm II: ADR - 45 mg/sqm iv on day 1; VCR - 1.2 mg/sqm iv on day 1; DBD - 140 mg/sqm po on days 1 through 10. Repeat course q 4 weeks.

Arm III: ADR, VCR as in Arm II. ICRF-159 - 250 mg/sqm/day po on days 1, 8 and 15 given in 3 divided doses. Repeat course q 4 weeks. Remove patients from study if disease progression is noted after 2 or more courses of Chemotherapy. (Arm discontinued, Addendum 2, March 1978)

Arm IV: DBD - 200 mg/sqm po on days 1 through 10 q 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; VCR - 1 and 5 mg vials; DBD - 50 and 100 mg tablets; ICRF-159 - 50 and 500 mg tablets.

DATE SUMMARIZED: 01/79
PATIENT ACCRUAL: 02360878

1.0014 HORMONAL THERAPY WITH TAMOXIFEN VS AMINOGLUTETHIMIDE AND DEXAMETHASONE VS ADRENALECTOMY FOR METASTATIC BREAST ADENOCARCINOMA

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PROTOCOL NUMBER(S) EST-2176

OBJECTIVES:

I. Compare tamoxifen vs. aminoglutethimide (Elipten) plus dexamethasone vs. surgical adrenalectomy in terms of objective tumor response rates and duration, survival times, time to treatment failure and associated morbidity for metastatic mammary adenocarcinoma.

II. Determine the response rate to surgical adrenalectomy for failures on the chemical agents.

PROTOCOL ENTRY CRITERIA: Female patients with histologically confirmed inoperable primary, recurrent or metastatic breast adenocarcinoma. Disease must be measurable and progressive. Menopause must have occurred at least 1 year prior to entry or surgical castration performed at least 12 weeks prior to entry. ECOG performance status of 3 or less and wbc greater than 4000, platelets greater than 100,000 and bilirubin of 3 or less. Patients with CNS metastases, lymphangitic metastases and peritoneal metastases with ascites are excluded.

PROTOCOL OUTLINE: Randomized study. Patients with performance status of 3 or who are ineligible for adrenalectomy are randomized between Arms II and III only. Patients with performance status of 0, 1, or 2 and who are candidates for adrenalectomy are randomized to Arms I, II or III. Nonresponders to therapy in Arm I are also randomized to Arms II or III.

Arm I: Surgery plus Hormonal Therapy. Adrenalectomy plus Cortisone, NSC-9703, Hydrocortisone, NSC-10483, or Dexamethasone, DM, NSC-34521. Florinef, NSC-15186, as needed.

Arm II: Hormonal Therapy. Aminoglutethimide (Elipten), no NSC number; DM.

Arm III: Hormonal Therapy. Tamoxifen, NSC-180973.

STRATIFICATION BY: Performance status 0, 1 vs. 2 vs. 3; presence or absence of liver and/or lung nodular metastases; castration response: curative, positive or unknown; short vs. long disease-free interval, eligibility for adrenalectomy; participating institutions.

SPECIAL STUDY PARAMETERS: Urine 17-hydroxycortisone, hormone receptors, immunologic skin tests, brain scan, bone survey.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, duration of response.

CURRENT STATUS: 132 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Surgical adrenalectomy. Cortisone - 40 mg/day po or Hydrocortisone - 40 mg/day po or Dexamethasone - 1.0 mg/day (AM) and 0.5 mg/day (PM), po. Florinef - 0.1 mg/day po, as needed. Evaluate at 12 weeks. Patients with progression, relapse or no change with deteriorating performance status may be randomized between Arms II and III. Follow responders until relapse or progression.

Arm II: Aminoglutethimide - 250 mg/day po; evaluate with weekly corticosteroid determinations during initial stabilization period. DM - 0.5 mg/day po; adjust dosage to prevent ACTH override. Evaluate at 12 weeks. Continue responders on treatment until progression or relapse. Nonresponders may be adrenalectomized.

Arm III: Tamoxifen - 8 mg/sqm po q 2 days. Evaluate at 12 weeks. Continue responders on treatment until progression or relapse. Nonresponders may be adrenalectomized.

Minimum treatment period for all arms is 4 weeks. Local palliative radiation therapy or palliative CNS irradiation may be administered.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Aminoglutethimide - 250 mg tablets; DM - 0.5 and 0.75 mg tablets; Tamoxifen - 2.5 and 10 mg tablets.

DATE SUMMARIZED: 02/77

1.0015 CAF (CTX/ADR/5-FU) WITH OR WITHOUT OOPHORECTOMY FOLLOWED BY MAINTENANCE WITH CMFP FOR METASTATIC OR INOPERABLE BREAST CANCER

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PROTOCOL NUMBER(S) EST-2177

OBJECTIVES:

I. Compare the efficacy of combination chemotherapy with CAF: cyclophosphamide (CTX), adriamycin (ADR), and 5-fluorouracil (5-FU), alone or in combination with oophorectomy as induction treatment followed by maintenance chemotherapy for responders with CMFP: CTX, 5-FU, methotrexate (MTX) and prednisone (PRED) for metastatic or inoperable breast cancer.

II. Determine the effectiveness for remission induction of CAF alone in estrogen receptor negative premenopausal patients. (Addendum 1, July 1978).

III. Compare time to progression and survival times of patients in each treatment.

IV. Evaluate the impact of potential prognostic variables upon the effects of each treatment.

PROTOCOL ENTRY CRITERIA: Premenopausal patients with evaluable or measurable disease of primary inoperable, recurrent or metastatic mammary adenocarcinoma, with positive estrogen receptor (ER). (Patients with negative ER are also eligible. Addendum 1, July 1978.) Patients must have adequate renal and hepatic functions and an ECOG performance status of 3 or better. Patients must be less than 50 years old if hysterectomized, or must have menstruated within the past 12 months, and may not have undergone radiation castration.

PROTOCOL OUTLINE: Randomized study - for ER positive, unknown or indeterminate patients. (Enter all ER negative patients to Arm II. Addendum 1, July 1978).

Arm I: Induction: Oophorectomy followed by 3-Drug Combination Chemotherapy. CAF: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Induction: 3-Drug Combination Chemotherapy. CAF, as in Arm I.

Maintenance: 3-Drug Combination plus Hormone Therapy. CMFP: CTX; 5-FU; Methotrexate, MTX, NSC-740; plus Prednisone, PRED, NSC-10023 (Substitute Fluoxymesterone, FXM, NSC-12165, for PRED, Addendum II, October 1978).

STRATIFICATION BY: ECOG performance status: 1 vs. 2 or 3; estrogen receptor status: positive vs. unknown vs. negative; disease dominance: visceral vs. osseous vs. other.

SPECIAL STUDY PARAMETERS: Liver and renal function tests; CEA; EKG; bone survey; mammogram of opposite breast; bone, liver and brain scans; bone marrow biopsy; ER measurements.

END POINTS: Response/remission rate, progression of disease, survival time, survival rate, objective tumor response, duration of response.

CURRENT STATUS: 108 patients are to be entered in about 3 years.

DOSAGE SCHEDULE:

Arm I: Induction: Oophorectomy followed within 28 days by Chemotherapy with: CTX - 100 mg/sqm po on days 1 through 14 q 28 days; ADR - 30 mg/sqm iv on days 1 and 8 q 28 days (total cumulative dose 500 mg/sqm); 5-FU - 500 mg/sqm iv on days 1 and 8 q 28 days.

Arm II: Induction: 3-Drug Combination Chemotherapy: CTX, ADR, 5-FU, as in Arm I.

Maintenance: Enter responders from Arms I or II after total ADR dose has been given (8 to 10 Induction courses) or any patient with prior cardiotoxicity. CTX - 100 mg/cm po on days 1 through 14; MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8; plus FXM - 20 mg/day po in 2 divided doses (Addendum 2, October, 1978). Repeat course q 28 days. Remove from study patients with disease progression after 28 days of Induction Chemotherapy. Enter patients in complete remission for 2 years to protocol EST-1177. Follow up all patients for life.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 50 mg tablets; 5-FU - 500 mg vials; MTX - 50 mg vials; ADR - 10 and 50 mg vials; PRED - 5 and 20 mg tablets; FXM - 5 mg tablets.

DATE SUMMARIZED: 10/78

PATIENT ACCRUAL: 00111178

1.0016 PHASE III HORMONE-MEDIATED THERAPY WITH ADRENALECTOMY, AMINOGLUTETHIMIDE, OR TAMOXIFEN FOR METASTATIC BREAST CANCER

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-4177

OBJECTIVES:

I. Compare efficacy of 3 hormono-manipulative therapies for metastatic breast cancer in women: adrenalectomy, surgical adrenalcortical suppression vs. aminoglutethimide, chemical adrenocortical suppression vs. tamoxifen, a chemical anti-estrogen agent.

II. Determine response rate to adrenalectomy for patients who fail on the chemical agents.

PROTOCOL ENTRY CRITERIA: Female patients with inoperable, recurrent or metastatic measurable or evaluable, progressive primary mammary adenocarcinoma who attained physiological menopause at least 1 year prior to study or were surgically castrated at least 12 weeks prior to study. Patients must have adequate hematologic, renal and hepatic function, and an ECOG performance status of at least 3 or else be willing and able to undergo major surgery. Patients must not have had sex hormone therapy for at least 4 weeks and corticosteroid therapy for at least 2 weeks prior to study; and patients must have progressive disease between cessation of either of these therapies and entry into study. Patients must be free of central nervous system, lymphangitic, or peritoneal (with ascites) metastases or history of neoplasm, and must have recovered from prior Chemotherapy and/or Radiotherapy.

PROTOCOL OUTLINE: Randomized study. Randomize patients with an ECOG performance status of 3 and nonresponders from Arm I to Arm II and III.

Arm I: Surgery plus Supportive Hormone Therapy. Adrenalectomy, plus Cortisone, NSC-9703, or Hydrocortisone, HC, NSC-10483 or Dexamethasone, DM, NSC-34521.

Arm II: 2-Drug Hormone Therapy. Aminoglutethimide, Elipten, no NSC number; DM.

Arm III: Single-agent Antihormone Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions, performance status, presence or absence of liver and/or lung-nodular metastases, castration response, duration of disease-free interval.

SPECIAL STUDY PARAMETERS: Urine 17-hydroxy corticoids and ketosteroids; estrogen receptor status; bone, liver, and brain scan; bone survey including entire spine, pelvis, femurs, and left lateral skull; skin tests for recall antigens.

END POINTS: Objective tumor response, length of survival, duration of response, toxicity/morbidity of treatment, response/remission rate.

CURRENT STATUS: About 132 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: Adrenalectomy plus Maintenance Corticoids: Cortisone - 50 mg/day po; or HC - 25-40 mg/day po; or DM - 1.5 mg/day po (1 mg in a.m. 0.5 mg in p.m.). Give Florinef - 0.1 mg/day po or q other day if needed to control hyponatremia.

Evaluate at 12 weeks. Minimal treatment and observation time is 4 weeks. Continue therapy for complete responders (CR), partial responders (PR) or patients with no change with nondeteriorating performance status (NC plus) until disease progression (PROG) or relapse (RLP). Rerandomize patients with PROG, RLP or with no change with deteriorating performance status (NC minus) to Arms II or III, and continue initial Maintenance corticoid therapy during treatment on Arm II or III.

Arm II: DM - 2 mg/day po in 4 divided doses, beginning 2 days prior to therapy with Elipten - 1000 mg/day po in 4 divided doses.

Arm III: TMX - 20 mg/day po in 2 divided doses.

Evaluate all Arm II or III patients at 12 weeks. Continue therapy for CR, PR and NC plus until PROG or RLP, encourage eligible patients with PROG, RLP or NC minus to cross over to Arm I for adrenalectomy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Aminoglutethimide - 250 mg tablets; DM - 0.5 and 0.75 mg tablets; TMX - 2.5 and 10 mg tablets.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00341178

1.0017 PHASE III ENDOCRINE THERAPY WITH AMINOGLUTETHIMIDE PLUS GLUCOCORTICOID (HC OR DM) VS TMX FOR METASTATIC BREAST CARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-4177R

OBJECTIVES:

I. Compare the effects of aminoglutethimide plus a glucocorticoid (hydrocortisone or dexamethasone) with those of tamoxifen on objective tumor response rates and durations, survival times, time to treatment failure, and associated morbidity in patients with advanced metastatic breast cancer.

II. Determine the response rate to the alternate therapy for patients who fail on the initial agent.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented inoperable, progressive, primary, recurrent or metastatic breast adenocarcinoma. Patients must have measurable or evaluable disease and an ECOG performance status of 3 or better. Physiologic menopause must have occurred at least 1 year prior to entry, or surgical castration must have been performed at least 12 weeks prior to entry, with evidence of progressive disease. Sex hormones or their derivatives must have been discontinued at least 4 weeks prior to entry and corticosteroids at least 2 weeks prior to entry. Patients must not have CNS metastases, lymphangitic metastases, and/or peritoneal metastases with ascites. There must be adequate bone marrow, renal, and hepatic function, and patients must not have had prior exposure to aminoglutethimide or tamoxifen.

PROTOCOL OUTLINE: Randomized study. After stratification, patients are randomized to Arm I or Arm II.

Arm I: Endocrine Therapy. Chemical adrenal cortical suppression. Aminoglutethimide, AGT, no NSC number; plus a glucocorticoid: Hydrocortisone, HC, NSC-10483; or Dexamethasone, DM, NSC-34521.

Arm II: Endocrine Therapy. Chemical antiestrogen. Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions, performance status (0-1 vs. 2-3), liver and/or lung-nodular metastases (present vs. absent), ER status (negative vs. positive vs. unknown), prior hormone response (positive vs. negative vs. no prior treatment or response unknown), duration of disease-free interval (more or less than 1 year), and prior adrenalectomy (yes vs. no).

SPECIAL STUDY PARAMETERS: Tumor measurements, hematological parameters, liver and kidney function tests, plasma dehydroepiandrosterone, liver and brain scans, bone scans, x-rays of bone scan lesions, chest x-ray.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 99 patients will be needed for each arm. There are (as of January 1980) 100 patients entered and at the present rate of 7 per month, another 14 months will be required for completion of accrual.

DOSAGE SCHEDULE:

Arm I: AGT - 1 g/day in 4 divided doses po beginning on day 3; plus HC or DM: HC - 20 mg at 8 AM, 12 PM, and 4 PM and 40 mg at 8 PM po on days 1-15, thereafter 40 mg/day in 4 divided doses; DM - 2 mg/day po in 4 divided doses on days 1 and 2, thereafter 3 mg/day in 4 divided doses. Minimum treatment period 4 weeks. Patients with stable disease or a response after 12 weeks will continue until progression or relapse. At relapse, treatment is stopped and glucocorticoid tapered to zero. After 2 weeks rest, qualified patients may be crossed to Arm II.

Arm II: TMX - 20 mg/day po in divided doses for 12 weeks unless progression occurs. Minimum treatment time is 4 weeks. Patients with stable disease or a response continue treatment until progression. At relapse, treatment stops and, after 2 weeks rest, patients may be crossed to Arm I if eligible.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AGT - 250 mg tablets; TMX - 2.5 and 10 mg tablets; HC - 20 mg tablets; DM - 0.5 mg tablets.

DATE SUMMARIZED: 07/80

1.0018 PHASE III CHEMOTHERAPY WITH CMF (CTX/MTX/5-FU) VS CMF PLUS PRED WITH OR WITHOUT TAMOXIFEN FOR STAGE II BREAST CANCER IN PREMENOPAUSAL WOMEN

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PROTOCOL NUMBER(S) EST-5177

OBJECTIVES:

I. Compare efficacy of chemotherapy with CMF - cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU) - to the same chemotherapy plus hormone therapy with prednisone (CMFP) with or without tamoxifen.

PROTOCOL ENTRY CRITERIA: Premenopausal, nonpregnant female patients who have undergone radical or modified radical mastectomy for potentially curable, movable, noninflammatory carcinoma in one breast only. Patients must have 1 or more histologically-proven, movable, tumor-positive axillary nodes and estrogen receptor content of tumor lesions must be known. Patients must have adequate hematologic, renal, and hepatic function and a normal bone scan. Patients must not have had previous treatment for the current malignancy; prior treatment for breast cancer; previous or concomitant malignancy; metastases other than the involved ipsilateral axillary nodes; preoperative ulceration or infiltration of skin greater than 2 cm, peau d' orange involving more than one-third of the breast, satellite or parasternal nodules, or edema of the arm.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. CMF: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. CMFP: CMF; plus Prednisone, PRED, NSC-10023.

Arm III: 3-Drug Combination Chemotherapy plus 2-Drug Hormone Therapy. CMFP; plus Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions; degree of nodal involvement: 1 to 3 vs. 4 or more; presence vs. absence of estrogen receptors.

SPECIAL STUDY PARAMETERS: Bone, liver and brain scan; xeromammogram or mammogram; estrogen binding, serum biological markers; hormone determinations.

END POINTS: Disease-free interval, length of survival, toxicity/morbidity of treatment, presence of tumor, recurrence rate, quality of survival.

CURRENT STATUS: Activated February 1978 (300-400 patients will be entered in about 2 years).

DOSAGE SCHEDULE: Begin therapy within 2 to 10 weeks of surgery.

Arm I: CMF: CTX - 100 mg/sqm po on days 1 through 14; MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8. Repeat course q 4 weeks, or when hematologic status permits.

Arm II: CMFP: CMF as in Arm I; plus PRED - 40 mg/sqm/day po on days 1 through 14. Repeat course q 4 weeks or when hematologic status permits.

Arm III: CMFP as in Arm II; plus TMX - 20 mg/day po in 2 divided doses for duration of treatment. Continue therapy for 12 four-week cycles or until evidence of treatment failure.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 50 mg tablets; MTX - 50 mg vials; 5-FU - 500 mg ampules; PRED - 5 mg tablets; TMX - 10 mg tablets.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00650978

1.0019 PHASE III CHEMOTHERAPY WITH CMFP (CTX/MTX/5-FU/PRED) VS CMFP PLUS TAMOXIFEN FOR STAGE II BREAST CANCER IN POSTMENOPAUSAL PATIENTS

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-6177

OBJECTIVES:

I. Compare the effectiveness of 1 year of adjuvant chemotherapy to no adjuvant chemotherapy for postmenopausal patients up to 65 years of age with Stage II breast cancer.

II. Compare the effectiveness of CMFP: cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU)/prednisone (PRED) to CMFP plus tamoxifen as adjuvant therapy for these patients.

III. Assess the importance of estrogen receptor protein status on: disease course; alteration of disease course by adjuvant chemotherapy; alteration of disease course by adjuvant chemotherapy plus hormone therapy, especially in respect to patients with estrogen receptor protein negative primary neoplasms.

IV. Encourage patients who participate in this protocol to participate in EST-1979. (Addendum 6, January 1980)

PROTOCOL ENTRY CRITERIA: Postmenopausal (greater than 1 year) patients up to 65 years of age having had radical or modified radical mastectomy less than 10 weeks prior to study for potentially curable, noninflammatory carcinoma confined to one breast or one breast and ipsilateral axilla only. Patient must have one or more histologically proven, tumor positive, axillary nodes, known estrogen receptor protein status, normal bone scan, and adequate renal, hepatic and hematologic function. Patients with previous oophorectomy must be at least 52 years of age. Patients must not have had previous treatment for current malignancy, including biopsy performed more than 4 weeks prior to the mastectomy, any previous or concomitant malignancy, any prior therapy for breast cancer, preoperative ulceration or infiltration of skin larger than 2 cm at greatest diameter or peau d'orange involving more than one-third of the breast.

PROTOCOL OUTLINE: Randomized study.

Arm I: No therapy.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. CMFP: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; plus Prednisone, PRED, NSC-10023.

Arm III: 3-Drug Combination Chemotherapy plus 2-Drug Hormone Therapy. CMFP; plus Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions; degree of nodal involvement: 1-3 vs. 4 or more; estrogen receptor status: positive vs. negative or indeterminate.

SPECIAL STUDY PARAMETERS: Bone, liver and brain scans; xeromammogram or mammogram; serum biological markers and hormone determinations.

END POINTS: Disease-free interval, survival rate, toxicity/morbidity of treatment, response/remission rate, recurrence rate.

CURRENT STATUS: 200-300 patients will be entered in about 2 years.

DOSAGE SCHEDULE: Start therapy 2-10 weeks after mastectomy. Repeat course q 28 days (or when counts return to wbc greater than 4000 and platelets greater than 100,000 if they have not reached that level at 28 days) for 12 courses. Calculate dosage from patient's ideal or actual body weight, whichever is less (Addendum 1, June 1978).

Arm I: No therapy.

Arm II: CMFP: CTX - 100 mg/sqm po on days 1 through 14; MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8; PRED -40 mg/sqm po on days 1 through 14.

Arm III: CMFP, as in Arm II; TMX - 20 mg/day po in 2 divided doses throughout study without modification, even when treatment is delayed because of reduced counts.

Follow all patients for life. Patients with disease progression are removed from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - 10 mg tablets; CTX - 50 mg tablets; MTX - 50 mg vials; 5-FU - 500 mg ampules; PRED - 5 mg tablets.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 00280778

1.0020 PHASE III HORMONE THERAPY WITH TMX BEFORE VS AFTER CMF (CTX/MTX/5-FU) FOR ADVANCED BREAST CANCER IN THE ELDERLY

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America

PROTOCOL NUMBER(S) EST-7177

OBJECTIVES:

I. Compare the activity of CMF - cyclophosphamide (CTX), methotrexate (MTX) and 5-fluorouracil (5-FU) to hormone therapy with tamoxifen (TMX) as to remission induction and response duration.

II. Establish the toxicity of CMF in the elderly patient utilizing creatinine clearance for initial dosage calculations.

III. Evaluate the toxicity of TMX in the elderly.

IV. Compare the effectiveness of hormone therapy followed by CMF vs. CMF followed by hormone therapy.

V. Correlate the activity of TMX and CMF with ER results, when tumor estrogen binding results are available.

VI. Evaluate the response to TMX in patients with prior hormone therapy.

VII. Compare the response rates of TMX vs. CMF therapy by tumor site.

PROTOCOL ENTRY CRITERIA: Patients 65 or older with measurable, histologically confirmed breast carcinoma, incurable by surgery. Patients must have adequate renal, hepatic and bone marrow functions and a performance status of 3 or better. Patients must have had no prior chemotherapy, nor prior radiotherapy to 50% or more of the pelvic bone structure and lower spine. Patients may have failed to respond to hormone therapy or have had disease progression after treatment was stopped.

PROTOCOL OUTLINE: Randomized study.

Arm I: Hormone Therapy followed upon progression by 3-Drug Combination Chemotherapy. Tamoxifen, TMX, NSC-180973; plus CMF: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 3-Drug Combination Chemotherapy followed upon progression by Hormone Therapy. CMF plus TMX.

STRATIFICATION BY: Performance status, dominant site of lesion, ER status, prior hormone therapy.

SPECIAL STUDY PARAMETERS: Renal and hepatic function tests, bone survey, bone scan, estrogen binding studies.

END POINTS: Response/remission rate, stability or progression or disease, objective tumor measurements, onset and duration of response.

CURRENT STATUS: About 236 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

Arm I: TMX - 20 mg/day po in 2 divided doses. Re-evaluate patients at 8 weeks and stop treatment for those who show progression of disease. Allow 10 or more days for hormone withdrawal. Crossover to Arm II patients showing no improvement or further progression.

Arm II: Daily dosages of CTX and MTX are not to exceed 100 mg/sqm po and 40 mg/sqm iv, respectively, and are adjusted by a factor based on renal status (creatinine clearance in ml/min divided by 70); CTX given on days 1 through 14 and MTX on days 1 and 8. 5-FU - 400 mg/sqm on days 1 and 8. Repeat cycle q 28 days. Re-evaluate patients at 8 weeks and crossover patients who show progression of disease to MTX therapy, as in Arm I.

Continue patients in both Arms until disease progression is documented, then remove from study. Follow all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - 10 mg tablets; CTX - 50 mg tablets; 5-FU - 500 mg vials; MTX - 50 mg vials.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00290878

1.0021 PHASE III CHEMOTHERAPY WITH CMFP (CTX/MTX/5-FU/PRED) AFTER VS DURING RADIOTHERAPY FOR NONRESECTABLE BREAST CARCINOMA

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PROTOCOL NUMBER(S) EST-8177

OBJECTIVES:

I. Compare optimal radiotherapy followed by chemotherapy with CMFP - cyclophosphamide (CTX), methotrexate (MTX), 5-fluorouracil (5-FU), and prednisone (PRED) vs. a combination of radiation therapy and chemotherapy. The radiation therapy will employ standard techniques with a so-called 'boost' to the primary tumor. Give chemotherapy in sequence with the radiation therapy (initiated pre- or postradiotherapy).

PROTOCOL ENTRY CRITERIA: Patients less than 70 years old with histologically confirmed mammary carcinoma, clinical stages T1b, T2b, T4a, T4b (greater than 2 cm ulceration), T4c and T4d with any N, MO. Patients must have a performance status of 3 or better, and no previous major surgery, Chemotherapy, Radiotherapy or Hormone Therapy for treatment of breast carcinoma. Patients must have adequate blood counts, renal and hepatic function and no history of breast cancer or other malignant neoplasms.

PROTOCOL OUTLINE: Randomized study.

Arm I: Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; Prednisone, PRED, NSC-10023. Radiotherapy: Cobalt-60 or linear accelerator x-rays, begin after initial Chemotherapy has been started.

Maintenance: 3-Drug Combination Chemotherapy plus Hormone Therapy. CMFP, as in Induction.

Arm II: Radiotherapy plus 2-Drug Combination Chemotherapy plus Hormone Therapy. Begin Radiotherapy prior to Chemotherapy. CMFP, as in Arm I.

STRATIFICATION BY: Good vs. poor risk (TNM stages of primary tumor, and involvement of regional lymph nodes); clinical and/or histological evidence of inflammatory breast carcinoma; menopausal status; measurability of disease.

SPECIAL STUDY PARAMETERS: Liver scan, mammogram, bone scan, breast biopsy, estrogen receptor protein assay.

END POINTS: Objective tumor response, disease-free survival, response/remission rate, toxicity/morbidity of treatment, survival rate, duration of response, rate of control of local disease.

CURRENT STATUS: 80 to 230 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Induction. Give 2-28 day courses prior to start of Radiotherapy. CTX - 100 mg/sqm po on days 1 through 14. MTX - 40 mg/sqm iv on days 1 and 8, 30 mg/sqm for patients 60 years and older. Reduce by 50% on day 8, cycle 3, and on days 1 and 8 of all further cycles administered during Radiotherapy. 5-FU - 600 mg/sqm iv on days 1 and 8, 400 mg/sqm for patients 60 years and older. Reduce by 50% on day 8, cycle 3, and on days 1 and 8 of all further cycles administered during Radiotherapy. PRED - 40 mg/sqm po on days 1 through 14. Repeat course q 28 days for at least 4 courses. Radiotherapy - begin on day 57 concurrently with the third course of Chemotherapy. Deliver at least 4000 rads to the breast and lymph nodes draining the breast with an additional 1000 to 1500 rads to the involved areas. Deliver entire course in 6 to 7 weeks for a maximal total dose not above 5500 rad. Give a minimum dose of 4000 rads within 5 to 6 weeks to the supraclavicular and to the axillary nodes (Addendum 1, June 1978).

Arm II: Radiotherapy: 5000 rads in 5 to 6 weeks followed immediately or in 1 to 3 weeks by a booster dose of 2000 to 3000 rads to the involved primary site and to draining lymphatics. Begin Chemotherapy as in Arm I 2 to 4 weeks after completion of Radiotherapy.

Re-evaluate patients in both Arms at 16 weeks. Enter responders or patients with stable disease to Maintenance Chemotherapy within 2 to 4 weeks of completion of Radiotherapy. Remove from treatment patients with local or distant disease progression and observe for disease progression at other sites and for survival.

Maintenance: Combination Chemotherapy with CMFP, as in Arm I, to a total of 18 cycles. Continue Chemotherapy for patients with residual tumor at that time until evidence of progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 50 mg tablets; 5-FU - 500 mg vials; MTX - 50 mg vials; PRED - 5 mg tablets.

DATE SUMMARIZED: 09/79

PATIENT ACCRUAL: 00370279

1.0022 PHASE II CHEMOTHERAPY WITH 5-FU/VCR/ADR/MITO FOR METASTATIC ADENOCARCINOMA OF THE BREAST

Carter, S. K., (415-497-7512) Northern California Oncology Group, 1801 Page Mill Rd., Bldg. B Suite 200, Palo Alto, California, 94304, United States of America
PROTOCOL NUMBER(S) NCOG-1B71

OBJECTIVES: This protocol replaces NCOG-P-1B71, a Phase I-II pilot study.

I. Evaluate the objective response rate for 5-fluorouracil (5-FU)/vincristine (VCR)/adriamycin (ADR)/mitomycin-C (MITO) combination chemotherapy both for CMF failures and for previously untreated patients.

II. Evaluate the mean and median duration of response.

III. Evaluate the toxicity of this regimen and establish a dosage range with acceptable toxicity.

PROTOCOL ENTRY CRITERIA: Patients less than 75 years old with histologically confirmed and measurable metastatic breast adenocarcinoma. Patients must have a Karnofsky performance of more than 50%, adequate renal and hematological status, and an estimated survival of at least 8 weeks. There must be no concomitant radiation therapy to bone nor prior chemotherapy with ADR or MITO.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: SMA-6, SMA-12, liver and bone scans.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 5 to 30 patients will be entered in 5 months.

DOSAGE SCHEDULE:

5-FU - 400 mg/sqm iv on days 1, 8, 29, 36; VCR - 1.0 mg/sqm (maximum single dose 2.0 mg) iv on days 1 and 29; ADR - 40 mg/sqm (maximum cumulative dose 450-550 mg/sqm) iv on days 1 and 29; MITO - 10 mg/sqm iv on day 1. Repeat course q 8 weeks. Remove from study patients with progression after at least one complete course. Continue therapy for complete or partial responders until evidence of disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; VCR - 1 and 5 mg ampules; ADR - 10 mg ampules; MITO - 5 mg vials.

DATE SUMMARIZED: 04/80

1.0023 PHASE II CHEMOTHERAPY WITH WEEKLY ADRIAMYCIN FOR INOPERABLE EXTENSIVE BREAST CANCER

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PROTOCOL NUMBER(S) NCOG-1B81

OBJECTIVES:

I. Evaluate efficacy and cardiac toxicity of weekly doses of single-agent chemotherapy with adriamycin for inoperable, extensive adenocarcinoma of the breast.

PROTOCOL ENTRY CRITERIA: Patients up to 75 years of age with histologically-confirmed, nonresectable for curative intent, locally recurrent or metastatic adenocarcinoma of the breast. Patients must have Karnofsky performance status of at least 60% and adequate liver, kidney, hematologic, and cardiac function. Patients must not have previous chemotherapy with protocol drug, or previous or concurrent irradiation which included a substantial part of the ventricles.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, kidney, liver, and cardiac function; bone scan; liver size; liver scan; liver ultrasound, or abdominal CT scan.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival time.

CURRENT STATUS: 21 patients will be entered in 1 to 2 years.

DOSAGE SCHEDULE:

ADR - 20 mg/sqm iv q 7 days. When cumulative dose of 450 mg/sqm is reached, evaluate patients with endomyocardial biopsy and cardiac catheterization, and continue therapy only if there is no cardiac toxicity. Remove from study patients showing no response.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules.

DATE SUMMARIZED: 11/79

1.0024 PHASE I-II EVALUATION OF AMSA/PRED/CLB FOR METASTATIC BREAST CARCINOMA PATIENTS WHO HAVE FAILED PRIOR ADR-CONTAINING REGIMENS

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PROTOCOL NUMBER(S) NCOG-1B92

OBJECTIVES:

I. Determine the efficacy of m-AMSA/prednisone/chlorambucil in patients with metastatic breast carcinoma who have failed on previous chemotherapy regimens including adriamycin.

II. Determine survival of responders and nonresponders on this regimen.

III. Determine the acute and chronic toxicities of this combination.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed breast carcinoma with documented metastatic disease. Patients must have evaluable disease and documented progressive disease following at least one complete cycle of chemotherapy regimens containing adriamycin, cyclophosphamide, and 5-fluorouracil. Patients must be under the age of 85 and must have adequate renal and bone marrow function. Patients must not have another active malignant disease or underlying cardiac disease that precludes the use of m-AMSA. Patients may not have had prior treatment with chlorambucil or m-AMSA nor may they be currently receiving radiotherapy to more than 50 percent of the marrow.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. m-AMSA, AMSA, NSC-249992; Prednisone, PRED, NSC-10023; Chlorambucil, CLB, NSC-3088.

STRATIFICATION BY: Karnofsky performance status (greater than 50 vs. 50 or less), extensive prior chemotherapy or radiotherapy (yes vs. no), bilirubin (2.0 mg percent or more vs. less than 2.0 mg percent), participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, tumor measurements, chest x-ray, bone scans and x-rays, bone marrow biopsy, liver scan or ultrasound or abdominal CT scan.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: An estimated 24-31 patients will be entered annually.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv infusion over 30 minutes on day 1; PRED - 40 mg/sqm/day po on days 1 through 7; CLB - 0.2 mg/kg/day po on days 1 through 7. Patients stratified as poor risk will receive AMSA at a reduced dosage: 90 mg/sqm. Cycles will repeat at 3-week intervals. Patients who progress after a minimum of 2 cycles will go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg vials; PRED - 1, 2.5, 5, and 20 mg tablets; CLB - 2 mg tablets.

DATE SUMMARIZED: 07/80

1.0025 L-PAM/5-FU WITH AND WITHOUT TMX FOR SURGICALLY 'CURABLE' BREAST CARCINOMA WITH ONE OR MORE POSITIVE AXILLARY NODES

Fisher, B., (412-624-2671) National Surgical Adj. Breast Project,
3550 Terrace St., Room 910A, Pittsburgh, Pennsylvania, 15261,
United States of America

PROTOCOL NUMBER(S) NSABP-B09; PBCTG-B09

OBJECTIVES:

I. Determine whether combination chemotherapy with melphalan, 5-fluorouracil plus tamoxifen adjuvant to surgery is more effective than surgery with melphalan plus 5-FU for breast carcinoma with one or more positive axillary nodes.

II. Determine whether tamoxifen in combination with melphalan plus 5-FU is more effective in patients whose tumors show positive estrogen receptor sites.

PROTOCOL ENTRY CRITERIA: Female patients, under 20 years of age, having had a radical or modified radical mastectomy for potentially curable breast cancer, with one or more tumor positive axillary nodes. Patients must not have previous or concomitant malignancy except effectively treated squamous or basal cell carcinoma of the skin; they must not have received prior therapy for breast cancer.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. Melphalan, L-PAM, NSC-8806; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. L-PAM; 5-FU; Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions; age; degree of nodal involvement.

SPECIAL STUDY PARAMETERS: Bone/liver/brain scan; skin tests; immunological parameters-lymphocyte blastogenesis, rosettes formation, immunoglobulin levels; opposite breast-mammogram, xeroradiogram, thermogram; estrogen binding.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, disease-free interval.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: L-PAM - 4 mg/sqm, po, for days 1 through 5 q 6 weeks; 5-FU - 300 mg/sqm, iv, for days 1 through 5 q 6 weeks.

Arm II: L-PAM and 5-FU - same as in Arm I. TMX - 10 mg, po, twice a day; continue throughout course of treatment or until relapse.

Begin Chemotherapy of both arms 2 to 4 weeks after mastectomy. Continue therapy until evidence of treatment failure is documented or for 17 six-week treatment cycles (approximately 2 years), whichever occurs first.

Dosage modifications for toxicity are given.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 01/77

PATIENT ACCRUAL: 09871278

1.0026 CHEMOTHERAPY WITH L-PAM/5-FU AND IMMUNOTHERAPY WITH C. PARVUM FOR NEW BREAST CARCINOMA WITH POSITIVE AXILLARY NODES

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3550 Terrace St., Room 910A, Pittsburgh, Pennsylvania, 15261,
United States of America

PROTOCOL NUMBER(S) NSABP-B10; PBCTG-B10

OBJECTIVES:

I. Test if C. parvum immunotherapy added to surgery and chemotherapy is more effective than surgery and chemotherapy alone.

II. Determine if there is prolongation in the disease-free interval of patients with primary breast cancer when C. parvum is administered along with chemotherapy.

III. Determine if tolerance to chemotherapy is augmented when C. parvum is added.

IV. Determine if C. parvum affects the biological parameters of a patient's immune status.

PROTOCOL ENTRY CRITERIA: Female patients, under 70 years of age, having had a radical or modified radical mastectomy for potentially curable carcinoma of the breast, having one or more histologically proven tumor positive axillary nodes. Patients must not have undergone prior therapy for breast cancer, or have previous or concomitant malignancy except squamous or basal cell carcinoma of the skin.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. Melphalan, L-PAM, NSC-8806; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 2-Drug Combination Chemotherapy plus Immunotherapy. L-PAM; 5-FU; plus Corynebacterium parvum, C. parvum, NSC-197213.

STRATIFICATION BY: Participating institutions, age, degree of nodal involvement - 1-3 or 4 or more positive axillary nodes.

SPECIAL STUDY PARAMETERS: Skin tests - PPD, Candida, Varidase, DNCB; immunological parameters - lymphocytes, blastogenesis, rosette formation, immunoglobulin levels; opposite breast - mammogram, thermogram, xeroradiogram; estrogen-binding protein; liver/brain scans.

END POINTS: Toxicity/morbidity of treatment, survival rate, duration of survival, disease-free interval.

CURRENT STATUS: About 300 patients will be entered.

DOSAGE SCHEDULE:

Arm I: L-PAM - 4 mg/sqm po on days 1 through 5 q 6 weeks; 5-FU - 300 mg/sqm iv on days 1 through 5 q 6 weeks.

Arm II: L-PAM and 5-FU as in Arm I. C. parvum - 2.5 mg/sqm, iv, q 3 weeks for 1 year, then q 6 weeks. Begin therapy of both arms 2 to 4 weeks after mastectomy. Continue therapy until evidence of treatment failure is documented or for 17 six-week treatment cycles, whichever occurs first.

Dosage modifications for toxicity are given.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 02/77

PATIENT ACCRUAL: 01491278

1.0027 COMPARISON OF TOTAL MASTECTOMY VERSUS SEGMENTAL MASTECTOMY WITH OR WITHOUT RADIOTHERAPY FOR CARCINOMA OF THE BREAST

Fisher, B., (412-624-2671) National Surgical Adj. Breast Project, 3550 Terrace St., Room 910A, Pittsburgh, Pennsylvania, 15261, United States of America

PROTOCOL NUMBER(S) NSABP-6; PBCTG-6; NSABP-B06

OBJECTIVES:

I. Compare the following therapeutic procedures in patients with breast cancer amenable to segmental mastectomy: A. Total mastectomy plus axillary dissection; B. Segmental mastectomy plus axillary dissection; C. Segmental mastectomy plus axillary dissection plus radiotherapy.

II. Evaluate the efficacy of melphalan chemotherapy on patients with positive axillary nodes who have been treated by one of the above surgical procedures, and the effects of this chemotherapy on the ovarian function of premenopausal patients.

III. Determine whether cosmetically acceptable preservation of the breast can be achieved without unfavorably influencing patient response, survival and morbidity.

IV. Determine the clinical significance of microscopic multicentricity of breast tumors.

PROTOCOL ENTRY CRITERIA: Patients with potentially curable breast carcinoma with tumors amenable to segmental mastectomy. Tumors must be confined to the breast and the ipsilateral axilla, must not exceed 4 cm in diameter, and must be freely movable. The breast must be of sufficient size to permit cosmetically acceptable resection.

PROTOCOL OUTLINE: Randomized study. All patients found to have positive axillary nodes upon histo-pathological examination following treatment in Arm I, II, or III enter Regimen A.

Arm I: Surgery. Total mastectomy plus axillary dissection.

Arm II: Surgery. Segmental mastectomy plus axillary dissection.

Arm III: Surgery plus Radiotherapy. Segmental mastectomy plus axillary dissection, followed by irradiation of the breast with Cobalt-60 or linear accelerator x-rays.

Regimen A: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

STRATIFICATION BY: Participating institutions, positive or negative clinical axillary nodal status, tumor size.

SPECIAL STUDY PARAMETERS: Skin tests: PPD, mumps, Candida, Varidase, DNCB. Frozen sections; thorough histo-pathological study of excised tumor tissues; serum biological markers; lymphocyte blastogenesis; rosette formation; immunoglobulin levels; estrogen binding protein. FSH, LH, estradiol and progesterone serum assays for premenopausal patients.

END POINTS: Toxicity/morbidity of treatment, survival rate, response/remission rate.

CURRENT STATUS: As of December 1979, 519 patients have been entered.

DOSAGE SCHEDULE:

Prior to surgery, patients may have skin tests, immunological survey and biological marker determinations, and at the time of mastectomy a tissue assay for estrogen binding protein may be performed. Following histological evaluation and prior to definitive surgery, randomize all patients to Arm I, II, or III.

Arm I: Total mastectomy plus axillary dissection.

Arm II: Segmental mastectomy plus axillary dissection.

Arm III: Segmental mastectomy plus axillary dissection plus Radiotherapy. Begin Radiotherapy 10 to 14 days but not more than 6 weeks following Surgery. Give a minimum of 5000 rads over 5 days to the breast area, including the entire scar of the breast.

Follow up all patients having negative nodes on pathological examination q 3 months for the first 3 years. All patients who have been treated with segmental mastectomy without irradiation who have recurrences in the ipsilateral breast will then be treated with total mastectomy. Enter patients with positive nodes on pathological examination to Regimen A.

Regimen A: L-PAM - 6 mg/sqm/day po for 5 days q 6 weeks. Begin treatment between 2 and 4 weeks following Surgery and continue therapy until evidence of treatment failure is documented or for 2 years, whichever occurs first. Follow up all patients on Chemotherapy q 6 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-PAM - 2 mg tablets.

DATE SUMMARIZED: 12/76

1.0028 RADIOTHERAPY FOR STAGE I AND STAGE II ADENOCARCINOMA OF THE BREAST

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) RTOG-7508

OBJECTIVES:

I. Determine the local controllability of adenocarcinoma of the breast by means of localized irradiation.

II. Determine the controllability of multifocal disease in the ipsilateral breast by localized irradiation.

III. Determine the disease-free interval.

IV. Study the influence of histology, histologic grade, menstrual status and other factors on ultimate prognosis.

V. Evaluate the complications of such therapy.

PROTOCOL ENTRY CRITERIA: Patients, under 75 years of age, with histological diagnosis of Stage I or Stage II, infiltrating ductal, comedo, colloid, medullary, lobular or papiliary adenocarcinoma of the breast. The disease must be localized to the breast, and the patients must not have received prior radiotherapy or chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. External.

Arm II: Radiotherapy. Combined external and interstitial.

STRATIFICATION BY: Participating institutions, histologic grade.

SPECIAL STUDY PARAMETERS: Bone evaluation.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response, disease-free interval, recurrence rate, appearance of metastasis, length and rate of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: External megavoltage irradiation. Dosage not given.

Arm II: External megavoltage irradiation plus interstitial irradiation. Dosage not given. Follow patients for survival.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/76

1.0029 PHASE II CHEMOTHERAPY WITH INOX FOR METASTATIC BREAST CANCER REFRACTORY TO STANDARD AGENTS

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America

PROTOCOL NUMBER(S) SEG-BRE-P48

OBJECTIVES:

I. Determine the response rate and the duration of response to inosine dialdehyde (INOX) in patients with measurable, metastatic, refractory breast cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven breast cancer that is not amenable to surgical or radiotherapeutic modalities and is refractory to standard therapy. Patients must be ineligible for higher priority SECSG protocols. Patients must be nonpregnant, older than 18 years, have a Karnofsky status of 50 percent or greater, and have adequate hematological, renal, and hepatic parameters. Patients must be free of another active malignancy or infection.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Inosine dialdehyde, INOX, NSC-118994.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurement, hematological assessment, liver and kidney function studies, CEA, clotting studies, chest and bone x-rays.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: About 29 patients will be entered.

DOSAGE SCHEDULE:

INOX - 1.5 mg/sqm iv over 6 hours on days 1 through 5, repeated q 28 days. Evaluate after 2 courses and remove from study when progression occurs.

Dosage modifications for toxicity are given.

DOSAGE FORMS: INOX - 500 mg vials.

DATE SUMMARIZED: 07/80

1.0030 PHASE III ADJUVANT CHEMOTHERAPY WITH CMF (CTX/MTX/5-FU) PLUS RADIATION VS SHORT OR LONG TERM CMF CHEMOTHERAPY FOR BREAST CARCINOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America

PROTOCOL NUMBER(S) SEG-76BRE0103; SEG-76BRE303

OBJECTIVES:

I. Compare the disease-free interval and survival of patients who, following radical mastectomy for carcinoma of the breast with positive axillary nodes, are randomized to either short-term chemotherapy with 6 cycles of CMF (cyclophosphamide, methotrexate, and 5-fluorouracil) or long-term chemotherapy with 12 cycles of CMF, or radiation therapy plus short-term chemotherapy with 6 cycles of CMF.

II. Compare the tolerance of each of these regimens and establish optimum duration of therapy.

PROTOCOL ENTRY CRITERIA: Patients with Stage II (International TNM classification) carcinoma of the breast with prior therapy restricted to radical mastectomy with one or more positive axillary nodes regardless of level, and who are free of metastatic foci. Patients will be entered within 56 days of surgery after complete healing of the wound.

PROTOCOL OUTLINE: Randomized study.

Arm I: Short-term 3-Drug Combination Chemotherapy. CMF: Cyclophosphamide; CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Long-term 3-Drug Combination Chemotherapy. CMF: CTX, MTX, 5-FU.

Arm III: Radiotherapy followed by Short-term 3-Drug Combination Chemotherapy. Radiotherapy with Megavoltage equipment; plus CMF: CTX; MTX; 5-FU.

STRATIFICATION BY: Participating institutions, post-menopausal status, interval following surgery (less than 28 days or 28-56 days), type of mastectomy (radical or modified radical) and number of histologically involved nodes (more or less than 4).

SPECIAL STUDY PARAMETERS: BUN, creatinine, total protein, albumin, uric acid, bilirubin, SGOT, LDH, alkaline phosphatase, calcium, bone scan and liver scan.

END POINTS: Response/remission rate, response duration, survival rate, toxicity/morbidity of treatment, duration of survival, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CMF: CTX - 100 mg/sqm po on days 1 through 14; MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8. Repeated q 4 weeks for 6 cycles.

Arm II: CMF as in Arm I, repeated q 4 weeks for 12 cycles.

Arm III: Radiation - Megavoltage with Cobalt-60 or linear accelerator - 200 rads given to chest wall/5 fraction/week for 4 1/2 to 5 weeks for a minimum of 4500 to 5000 rads; 4500 rads at 3-cm depth given separately to skin and to interval mammary nodes. 900-1000 rads/5 fractions/week given to axillary lymph nodes. 4500 rads minimum at rate of 900-1000 rads/5 fractions/week at 3-cm depth given to supraclavicular area. Upon completion of Radiotherapy, give CMF: CTX - 75 mg/sqm po days 1 to 14; MTX - 30 mg/sqm iv day 1 and day 8; 5-FU - 450 mg/sqm iv days 1 and 8. Repeated q 4 weeks for 2 cycles; then CMF as in Arm II q 4 weeks for 4 cycles.

Dosage modifications for toxicity are given as indicated by RBC, granulocyte and platelet count and by Hb, bilirubin and creatinine clearance.

DOSAGE FORMS: CTX - 25 and 50 mg tablets; MTX - 5 and 50 mg vials; 5-FU - 10 ml ampules.

DATE SUMMARIZED: 12/76

PATIENT ACCRUAL: 02001078

1.0031 CHEMOTHERAPY WITH CAF VS CAF ALTERNATING WITH CAMELEON FOR METASTATIC BREAST CARCINOMA

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PROTOCOL NUMBER(S) SEG-77BRE0103; SEG-77BR324

OBJECTIVES:

I. Significantly increase the duration of disease control (time to initiation of alternative therapy) over that achievable with CAF: cyclophosphamide (CTX), adriamycin (ADR), and 5-fluorouracil (5-FU) by a sequentially alternating regimen of CAF and CAMELEON: cytosine arabinoside (ARA-C), methotrexate (MTX), citrovorum factor (CF), and vincristine (VCR) in 'poor risk' patients with metastatic breast cancer.

II. Increase the response rate of such patients by 30% or more.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-confirmed measurable carcinoma of the breast but no other serious malignancy. Patients are considered 'poor risk' because of metastatic site: liver, lymphangitic, pleural effusion or pulmonary nodules. Patients must not have received prior chemotherapy with study agents and must have adequate blood counts and renal function.

PROTOCOL OUTLINE: Randomized study. Enter 1 patient to Arm I to each 3 patients entered to Arm II.

Arm I: 3-Drug Combination Chemotherapy. CAF: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 3-Drug Combination Chemotherapy alternating with 4-Drug Combination Chemotherapy. CAF: CTX, ADR, 5-FU, alternating with CAMELEON: Cytosine arabinoside, ARA-C, NSC-63878; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590; Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Participating institutions, Karnofsky performance status, site of metastasis.

SPECIAL STUDY PARAMETERS: Hepatic and renal function tests; CEA; bone, liver and brain scans, ER status if available.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival.

CURRENT STATUS: 170 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Arm I: CTX - 500 mg/sqm iv on day 1; ADR - 50 mg/sqm iv (maximum cumulative dose 450 mg/sqm) on day 1; 5-FU - 500 mg/sqm iv on day 1. Repeat course q 3 weeks for one year, terminating ADR therapy when maximum dose has been given.

Arm II: CTX, ADR, 5-FU as in Arm I repeated q 6 weeks; plus VCR -1 mg iv on days 1, 2, 29, 36; MTX - 30 mg/sqm po in 4 divided doses immediately following VCR administration on days 22, 29, 36; ARA-C - 300 mg/sqm iv, 24 hours after MTX on days 23, 30, 37; CF - 25 mg po in 4 divided doses starting 6 hours after ARA-C on days 23, 30, 37. Repeat entire cycle q 6 weeks for a total of one year.

Follow up all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; ADR - 10 and 50 mg vials; 5-FU - 500 mg ampules; ARA-C - 100 and 500 mg vials; MTX - 2.5 and 50 mg tablets; CF - 5 mg tablets; VCR - 1 and 5 mg ampules.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00170178

1.0032 CYCLOPHOSPHAMIDE/ADRIAMYCIN/5-FLUOROURACIL WITH AND WITHOUT LEVAMISOLE IMMUNOTHERAPY FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) SEG-78BRE0203; SEG-78BRE337

OBJECTIVES:

I. Evaluate the effectiveness of levamisole in prolonging the duration of response and survival of 'good risk' patients with metastatic breast cancer treated with the combination of cyclophosphamide, adriamycin, and fluorouracil.

PROTOCOL ENTRY CRITERIA: Patients with breast cancer metastases confined to bone (Pattern 1) and/or local anterior chest wlal and/or ipsilateral supraclavicular or axillary nodes (Pattern 2). Patients must have adequate bone marrow reserve and must not have had prior treatment with cytotoxic drugs. Patients with positive estrogen receptor status must have had or refused prior hormone therapy, additive or ablative.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Immunotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893; plus Levamisole, LEV, NSC-177023.

Arm II: 3-Drug Combination Chemotherapy. CTX, ADR, 5-FU plus placebo.

STRATIFICATION BY: Participating institutions; metastasis: bone (Pattern 1) vs. local skin and node (Pattern 2); prior hormone therapy; bone disease.

SPECIAL STUDY PARAMETERS: Liver and bone scan, skeletal x-ray, photography.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: 150 patients will be entered in about 1 1/2 to 2 years.

DOSAGE SCHEDULE:

Arm I: CTX - 250 mg/sqm; ADR - 25 mg/sqm; 5-FU - 250 mg/sqm; all given iv q 3 weeks with 50% escalation of dose for second course and 100% escalation of dose for third course if toxicity permits. Repeat third course once. LEV - 2.5 mg/kg po on days 4, 5, 11, 12, 18 and 19 q 3 weeks.

Evaluate after fourth course. Continue therapy for patients with partial or complete response until total cumulative dose of ADR reaches 450 mg/sqm, then continue with LEV therapy only until disease progression. Remove patients without response from study.

Arm II: CTX, ADR, 5-FU as in Arm I. Placebo, as LEV in Arm I. Evaluate and continue therapy as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: LEV - 50 mg tablets; ADR - 10 and 50 mg vials; 5-FU - 10 cc ampules; CTX - 100, 200 and 500 mg vials, 50 mg tablets. Placebo - identical to LEV tablets.

DATE SUMMARIZED: 10/78

1.0033 PHASE III DES VS TMX FOR POSTMENOPAUSAL ER POSITIVE OR ER UNKNOWN METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) SEG-79BRE334

OBJECTIVES:

I. Compare the response in ER positive and ER unknown postmenopausal metastatic breast cancer patients to treatment with either diethylstilbestrol or tamoxifen.

II. Compare the median durations of response of the two drugs.

III. Determine whether patients who initially responded to one of the drugs show a further response to the alternate agent at the time of relapse.

IV. Determine whether those patients who do not respond to one of the drugs will respond to the other.

V. Determine whether a tamoxifen regression may occur.

PROTOCOL ENTRY CRITERIA: Patients with advanced breast cancer not considered curable by surgery or radiation therapy. Patients younger than 70 years will not be accepted unless they are ineligible for participation in other first priority SECSG studies. Patients must be ER positive or ER status unknown and must not have received estrogens or anti-estrogens since the diagnosis of breast cancer.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Hormone Therapy. Diethylstilbestrol, DES, NSC-3070.

Arm II: Single-agent Antiestrogen Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions; dominant disease site: bone vs. soft tissue vs. visceral; ER status: positive vs. unknown; prior endocrine therapy; prior chemotherapy.

SPECIAL STUDY PARAMETERS: Tumor measurements, liver and kidney functions tests, chest x-ray, liver scan, bone survey.

END POINTS: Response/remission rate, duration of response, objective tumor response.

CURRENT STATUS: 60 evaluable patients will be entered onto each arm.

DOSAGE SCHEDULE:

Arm I: DES - 15 mg/day po in 3 divided doses for at least 4 weeks.

Arm II: TMX - 20 mg/day po in 2 divided doses for at least 4 weeks.

If after 4 weeks the patient is stable or showing tumor regression, treatment will be continued until progressive disease is seen. Patients who initially respond and then progress will be observed off treatment for an estrogen or TMX withdrawal regression. Treatment will continue to be withheld until progression occurs in those who are stable or showing regression. At the time of renewed progression the patient will be started on the alternate drug. If there is no response to initial hormone treatment, the patient will be crossed over to the alternate drug when progressive disease is demonstrated. When progression occurs on the alternate drug, patients will be observed off treatment for 4 weeks for withdrawal regression if an initial response was seen. Patients will be off study when progressive disease is documented.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DES - 5 mg tablets; TMX - 10 mg tablets.

DATE SUMMARIZED: 05/80

1.0034 MEDICAL ADRENALECTOMY WITH AMINOGLUTETHIMIDE AND DM WITH OR WITHOUT CAF (CTX/ADR/5-FU) FOR ER-POSITIVE METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) SEG-80BRE370

OBJECTIVES:

I. Determine in a Phase III randomized trial the response rate to medical adrenalectomy with aminoglutethimide and dexamethasone as initial therapy for ER-positive metastatic breast cancer.

II. Determine whether the addition of 5 cycles of CAF (cyclophosphamide, adriamycin, and 5-fluorouracil) to medical adrenalectomy significantly increases the response rate over medical adrenalectomy alone in these patients.

III. Compare the duration of response and survival of patients receiving 5 cycles of CAF in addition to medical adrenalectomy with the duration of response and survival of patients receiving medical adrenalectomy alone initially, followed by CAF at the time of progression.

PROTOCOL ENTRY CRITERIA: Patients with documented metastatic breast carcinoma of either good or poor risk by SECSG with measurable disease and with ER protein levels of greater than 7 fmol/mg cytoplasmic protein. Patients may have received prior hormonal therapy, but progression of disease must have been documented at least 4 weeks after cessation of hormonal therapy. Patients must not have had prior surgical ablative hormonal therapy other than oophorectomy, may not be over 70 years of age, must have adequate hematological parameters and a performance status of at least 50 percent, and must not have had prior therapy with adriamycin. Patients who have received prior adjuvant postoperative therapy with 1-phenylalanine mustard, cyclophosphamide, methotrexate, or 5-fluorouracil will be eligible providing they did not relapse while receiving adjuvant therapy or within 6 months of completing therapy.

PROTOCOL OUTLINE: Randomized study.

All premenopausal patients will undergo surgical oophorectomy.

Arm I: Medical Adrenalectomy. Aminoglutethimide, AGT, no NSC number; Dexamethasone, DM, NSC-34521.

Arm II: Medical Adrenalectomy plus 3-Drug Combination Chemotherapy. AGT; DM; plus CAF: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; and 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Participating institutions; menopausal status; prognostic disease category (presence vs. absence of liver, pleural, or lymphangitic pulmonary metastasis); prior therapy with estrogen, androgen, progestin, anti-estrogen, or corticosteroids vs. no prior hormonal therapy.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function studies, tumor measurements, liver and bone scans, skeletal x-ray, T4, and plasma cortisol.

END POINTS: Response/remission rate, duration of response, toxicity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: About 176 cases will be entered in a 3-year period.

DOSAGE SCHEDULE:

Arm I: AGT - 1 g/day po in 4 divided doses; DM - 3 mg/day in 2 divided doses. Therapy will begin 7-28 days after surgical oophorectomy and will be continued until progression of disease, at which time CAF therapy will be instituted at 3-week intervals as described in Arm II, and patients will be followed for duration of survival.

Arm II: AGT and DM as in Arm I; CAF: ADR - 50 mg/sqm iv; CTX - 500 mg/sqm iv; 5-FU - 500 mg/sqm iv. CAF therapy repeated q 3 weeks for a total of 5 courses, with the total cumulative dose of ADR not to exceed 450 mg/sqm. Patients will then continue on AGT and DM and be followed for duration of response. If progressive disease occurs prior to administration of the fifth course of CAF, therapy will be discontinued and treatment will be at the discretion of the investigator. All patients will be followed for duration of survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AGT - 250 mg tablets; CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; 5-FU - 500 mg ampules; DM - 0.5 mg tablets.

DATE SUMMARIZED: 06/80

1.0035 PHASE II STUDY OF TAMOXIFEN, ABLATIVE SURGERY, AND CTX/5-FU/ADR CHEMOTHERAPY FOR RECURRENT CARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) SWOG-7632

OBJECTIVES:

I. Establish the survival of breast cancer patients when treating the first recurrence with a coordinated hormonal chemotherapeutic approach.

II. Determine the efficacy of a response to tamoxifen in predicting response to ablative surgery.

III. Correlate hormonal manipulations with estrogen and progesterone receptors where possible.

PROTOCOL ENTRY CRITERIA: Patients with non-metastasized cancer of the breast, first recurrence only, who have been surgically and/or radiotherapeutically treated for cure of primary disease, who have had no prior treatment with adriamycin, and who are estrogen receptor positive. Patients who have received birth control pills or estrogen prior to diagnosis, and patients who have undergone castration within 1 month of mastectomy, are eligible.

PROTOCOL OUTLINE: Enter patients with no prior castration to Regimen A. Enter patients with prior castration to Regimen B. Enter or randomize nonresponders or patients who relapse to Arms I and II as indicated. (Postmenopausal patients responsive to Tamoxifen subsequently receive adrenalectomy or hypophysectomy plus oophorectomy plus Tamoxifen. Amendment 1, October 1979.)

Regimen A: Single-agent Hormone Therapy plus Surgery. Tamoxifen, TMX, NSC-180973; plus Oophorectomy.

Regimen B: Single-agent Hormone Therapy. TMX.

Arm I: Surgery. Adrenalectomy or hypophysectomy.

Arm II: 3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Participating institutions, menopausal status.

SPECIAL STUDY PARAMETERS: Estrogen receptors.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 150 patients per year will be entered over 32 months.

DOSAGE SCHEDULE:

Regimen A: TMX - 20 mg/day po in 2 divided doses. Evaluate at 3 and 10 weeks, continuing responders and patients with acceptable stable disease on TMX alone until relapse. For nonresponders, patients who relapse, and patients with unacceptable stable disease, perform oophorectomy with continued TMX. On reevaluation, enter patients who show no response to TMX alone and also fail to respond to TMX plus oophorectomy to Arm II. Randomize patients who responded to TMX alone but did not respond to TMX plus oophorectomy to Arms I or II. Enter patients who relapse following initial response to both modalities to Arm I.

Regimen B: TMX - 20 mg/day po in 2 divided doses. Evaluate at 3 weeks. Enter nonresponders to Arm II. Continue responders and patients with acceptable stable disease to relapse, then enter to Arm I.

Arm I: Adrenalectomy or hypophysectomy. Enter nonresponders and patients who relapse to Arm II.

Arm II: For patients with no prior Chemotherapy or only adjuvant melphalan: ADR - 40 mg/sqm iv, on day 1; CTX - 200 mg/sqm/day po on days 3 through 6; 5-FU - 400 mg/sqm iv on days 1 and 8. Repeat course q 3 weeks. For patients with prior adjuvant Chemotherapy with CMF or COMP-FU: ADR - 60 mg/sqm iv on day 1 q 3 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - 10 mg tablets; ADR - 10 mg vials; CTX - 100, 200 and 500 mg vials; 5-FU - 500 mg vials.

DATE SUMMARIZED: 12/77

PATIENT ACCRUAL: 00661277

1.0036 OOPHORECTOMY, CMFVP, AND TMX COMBINED MODALITY ADJUVANT THERAPIES FOR ER POSITIVE AND ER NEGATIVE STAGE II BREAST CANCER

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PROTOCOL NUMBER(S) SWOG-7827

OBJECTIVES:

I. Compare the effects of combination chemotherapy with CMFVP: cyclophosphamide/methotexate/5-fluorouracil/vincristine/prednisone vs. CMFVP plus oophorectomy as adjuvant therapy following mastectomy for premenopausal, estrogen-receptor-positive (ER positive) women with Stage II breast cancer.

II. Compare the effects of CMFVP plus tamoxifen (TMX) vs. TMX in postmenopausal, ER negative women with Stage II disease.

III. Compare the effects of CMFVP for 1 year vs. 2 years in all ER negative (ER-) women with Stage II disease.

IV. Correlate ER status with disease-free interval and survival.

PROTOCOL ENTRY CRITERIA: Female patients with histologically confirmed breast cancer with 1 or more pathologically proven, involved axillary node (Stage II - T0-1N1b,T2bN1a or b) who have had a radical or modified radical mastectomy with complete removal of primary neoplasm and clinically apparent axillary disease no more than 6 weeks prior to entry. Patients must have had movable primary and axillary disease, estrogen receptor status determined, and adequate cardiac, liver and kidney function. Patients must not have had metastatic disease or involvement of other breast nor prior hormonal or chemotherapy.

PROTOCOL OUTLINE: Randomized study. Randomize all ER negative patients to Arms I or II. Randomize ER positive premenopausal patients to Arms I or III. Randomize ER positive postmenopausal patients to Arms I, IV, or V.

Arm I: 4-Drug Combination Chemotherapy plus Hormone Therapy. CMFVP: Cyclophosphamide, CTX, NSC-262271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-198893; Vincristine, VCR, NSC-67574; plus Prednisone, PRED, NSC-10023.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy followed by Single-agent Chemotherapy plus Hormone Therapy. CMFVP, as in Arm I, for 1 year followed by VCR, PRED for 1 year.

Arm III: 4-Drug Combination Chemotherapy plus Hormone Therapy plus Surgery. CMFVP; plus oophorectomy.

Arm IV: 4-Drug Combination Chemotherapy plus Hormone plus Antiestrogen Therapy. CMFVP; plus Tamoxifen, TMX, NSC-180973.

Arm V: Anti-estrogen Therapy. TMX.

STRATIFICATION: Participating institutions; premenopausal vs. postmenopausal status; number of positive axillary nodes: 1 to 3 vs. 4 or more; postoperative radiotherapy; size of primary tumor: less than 2 cm vs. 2 to 5 cm.

SPECIAL STUDY PARAMETERS: Bone, liver, and brain scan (or CAT); estrogen receptor assay; mammogram of remaining breast; plasma FSM; estradiol and estrone.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, survival time.

CURRENT STATUS: A minimum of 280 patients will be entered in about 5 years.

DOSAGE SCHEDULE:

Begin Chemotherapy within 2 to 6 weeks following mastectomy. Perform oophorectomy no later than 4 weeks after mastectomy, and start Chemotherapy 10 to 20 days thereafter. Give 10 weeks of Chemotherapy prior to postoperative Radiotherapy.

Arm I: CMFVP: CTX - 60 mg/sqm/day po; MTX - 15 mg/sqm iv q 7 days; 5-FU - 400 mg/sqm iv q 7 days; VCR - 0.625 mg/sqm q 7 days for 10 weeks; PRED - 30 mg/sqm po on days 1 through 14 and 29 through 42, 20 mg/sqm po on days 15 through 28. Continue therapy for 1 year.

Arm II: CMFVP therapy as in Arm I for 1 year, followed by VCR; PRED as in Arm I for the second year.

Arm III: CMFVP as in Arm I; plus oophorectomy.

Arm IV: CMFVP as in Arm I; TMX - 20 mg/day po in 2 divided doses for 1 year.

Arm V: TMX - as in Arm IV.

Remove from study patients with metastases or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 mg vials; CTX - 50 mg tablets; 5-FU - 500 mg vials; MTX - 5 and 50 mg vials; PRED - 5 and 50 mg tablets; TMX - 10 mg vials.

DATE SUMMARIZED: 11/79

1.0037 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR RESISTANT METASTATIC CARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) SWOG-7921

OBJECTIVES:

I. Determine the response rate and remission duration with weekly intravenous therapy using methyl-GAG (MGBG) in patients with carcinoma of the breast who have failed on higher priority treatment protocols.

II. Define the qualitative and quantitative toxicity of this regimen.

PROTOCOL ENTRY CRITERIA: Patients with measurable histologically proven incurable advanced metastatic carcinoma of the breast. Patients must have a minimum life expectancy of 6 weeks and a Karnofsky performance status of 50 to 60. Patients must have adequate renal, hepatic and bone marrow function. Four weeks must have elapsed since prior therapy, with hematologic recovery.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MGBG, NSC-32946.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, remission duration, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: At least 25 patients will be entered.

DOSAGE SCHEDULE:

MGBG - 600 mg/sqm iv infusion on day 1 q 7 days for a minimum of 3 courses. Increase dose 100 mg/sqm each course maintaining wbc above 3,000 and platelets above 100,000 and decreasing dosage for stomatitis. Remove patients with unacceptable toxicity or progressive disease after 3 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

1.0038 PHASE III COMBINATION CHEMOTHERAPY WITH CMFV (CTX/MTX/5-FU/VCR) FOR ER- BREAST CANCER

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PROTOCOL NUMBER(S) SWOG-7985

OBJECTIVES:

I. Compare disease-free interval and survival among control group Stage I (and Stage II node negative) breast cancer patients whose tumors are determined to be ER- at the time of mastectomy, versus Stage I (and Stage II node negative) ER- patients treated with adjuvant CMFV: cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU)/vincristine (VCR) for 6 months.

II. Document recurrence patterns among untreated patients with Stage I breast cancer whose tumors are determined to be ER- at the time of mastectomy.

PROTOCOL ENTRY CRITERIA: Patients must have undergone a radical, modified radical or total mastectomy, or segmental mastectomy with axillary node dissection for potentially curable, histologically proven breast carcinoma (Stage I or II, node negative). Estrogen receptor assay on the primary tumor must be less than 10 femtomoles/mg cytosol protein. The primary tumor must be 5 cm or less in diameter, and must not be fixed to the chest wall. Pathological staging must be T1 or T2, N0 M0. Patients must have adequate hematologic and renal function. Not eligible are patients with malignant breast tumors other than carcinoma or inflammatory carcinoma, and those with bilateral malignancies, nodal metastases, evidence of distant metastases, or previous or concomitant malignancy (other than basal cell or squamous cell carcinoma of the skin). Patients who are pregnant or lactating, or who have received previous treatment for their current malignancy, are not eligible. Patients who have undergone a segmental mastectomy may receive post-operative radiation therapy only as outlined in the protocol.

PROTOCOL OUTLINE: Randomized study. Patients must be registered/randomized within 28 days of mastectomy.

Arm I: No further treatment until relapse.

Arm II: 4-Drug Combination Chemotherapy. CMFV: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Extent of tumor, menopausal status, prior therapy.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Disease-free interval, toxicity/morbidity of treatment.

CURRENT STATUS: 152 patients minimum requirement, 76 on each arm; accrual rate estimated at 5 patients/month, or patient entry of approximately 3 years.

DOSAGE SCHEDULE:

Arm II: CTX - 600 mg/sqm iv day 1; MTX - 30 mg/sqm iv day 1; 5-FU - 450 mg/sqm iv days 1 and 8; VCR - 1 mg day 1. Courses repeated q 21 days, provided WBCs are greater than 3,000 and platelets greater than 100,000. Treatment will be terminated at 6 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 50 mg tablets; MTX - 5 and 50 mg vials; 5-FU - 500 mg vials; VCR - 1 and 5 mg vials.

DATE SUMMARIZED: 05/80

1.0039 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE FOR REFRACTORY BREAST CANCER

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PROTOCOL NUMBER(S) SWOG-8008

OBJECTIVES:

I. Determine the response rate and remission duration in patients with refractory breast cancer treated with dihydroxyanthracenedione on a single dose, every-three-week schedule.

II. Define the qualitative and quantitative toxicities of dihydroxyanthracenedione in a Phase II study.

PROTOCOL ENTRY CRITERIA: Patients with pathologically verified histologic diagnosis of advanced breast cancer with measurable disease, who are ineligible for studies of higher priority. The WBC count must be 3000/cumm or greater, and platelet count 100, 000/cumm or greater. Patients must be past the nadir resulting from previous therapy, particularly therapy with nitrosoureas or mitomycin-C. Serum creatinine and bilirubin must be 2 mg percent or less. The performance status must be 3 or better (SWOG criteria).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Participating institutions; prognostic risk: good vs. poor; prior chemotherapy with adriamycin: yes vs. no.

SPECIAL STUDY PARAMETERS: Fasting blood sugars, chest x-ray, EKG, tumor scans or x-ray measurement, CBC and platelets.

END POINTS: Response/remission rates, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 14-25 patients will be entered.

DOSAGE SCHEDULE:

DHAD - 12 mg/sqm through a free-running iv over 30 minutes q 3 weeks for good-risk patients (those 65 years of age or younger with no or limited prior Radiotherapy, good tolerance to prior Chemotherapy, WBC at least 4000/cumm, and platelets at least 100,000/cumm). Poor-risk patients (those over 65 years of age or those with extensive Radiotherapy, i.e., to more than 33 percent of bone marrow, poor tolerance to prior Chemotherapy or WBC at least 3000/cumm and platelets at least 100,000/cumm) receive DHAD - 10 mg/sqm through a free-running iv over 30 minutes q 3 weeks. Patients with progressive disease after 2 courses go off study. Those who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 5 mg ampules.

DATE SUMMARIZED: 10/80

1.0040 PHASE III RADICAL SURGERY VS LOCAL EXCISION PLUS RADIOTHERAPY FOR BREAST CARCINOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-8027

OBJECTIVES:

I. Document recurrence rates, patterns of recurrence, and survival among patients with Stage I or Stage II node-negative breast cancer whose tumors are determined to be estrogen-receptor-positive at the time of surgery.

PROTOCOL ENTRY CRITERIA: Women with Stage I or II node-negative nonmetastatic histologically proven breast carcinoma who have had a radical, modified radical or adequate local excision with axillary node dissection. The estrogen receptor assay on the primary tumor must be positive. The interval between surgery and protocol entry must not be greater than 6 weeks for patients with radical or modified radical surgery or 21 days for patients with adequate local excision. The general health of the patients must be adequate, and there must be no previous or concomitant malignancy except for adequately treated basal or squamous cell carcinoma of the skin or carcinoma of the cervix in situ.

PROTOCOL OUTLINE: Nonrandomized study. Patients who have undergone radical or modified radical mastectomy enter Regimen A; those who have undergone local excision and axillary node dissection enter Regimen B.

Regimen A: No further treatment.

Regimen B: Radiotherapy. Co-60 or supervoltage equipment generating minimum peak energy of 2 MeV.

STRATIFICATION BY: Tumor size: less than 2 cm vs. 2-5 cm; menopausal status: pre vs post; type of surgery: mastectomy vs. lumpectomy plus radiotherapy.

SPECIAL STUDY PARAMETERS: Hematologic function tests, SMA-12, urinalysis, plasma FSH, plasma LH, estradiol and estrone, chest x-ray, bone and liver scans, brain or CAT scan, mammogram of remaining breast.

END POINTS: Recurrence rate, patterns of recurrence, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Radical excision consisting of the removal of the breast, pectoralis muscles and axillary contents en bloc; or modified radical excision consisting of total removal of breast tissue with axillary node dissection in continuity, removal of pectoralis fascia but not the pectoralis muscle, removal or detachment from the insertion of the pectoralis minor muscles. Patients enter the protocol within 21 days after Surgery and are observed only.

Regimen B: Adequate local excision with node dissection consisting of local excision of tumor with a small rim of normal breast tissue with dissection of lower and middle axillary nodes. Between 14 and 21 days following surgery, begin Radiotherapy: 4500-5000 rads in 5 to 5.5 weeks at the rate of 180-200 rads/day to the breast and chest wall. Patients who have had only a wide excision of grossly palpable disease may receive supplemental boost irradiation with reduced tangential photon fields, electron beam or interstitial technique such as Iridium 192. Doses for additional boost therapy should range between 1500 and 2000 rads.

Patients will be evaluated q 6 months until death, or for a minimum of 10 years. Patients who develop unacceptable toxicity from Radiotherapy will go off study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/80

1.0041 COMBINATION CHEMOTHERAPY WITH CTX/ADR/5-FU PLUS MASTECTOMY FOR STAGE III BREAST CARCINOMA

Aisner, J., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America

PROTOCOL NUMBER(S) BCRP-7814

OBJECTIVES:

I. Evaluate the efficacy of preoperative chemotherapy with cyclophosphamide/adriamycin/5-fluorouracil to shrink primary masses and thus make them technically more amenable to resection and avoid the use of skin grafts in patients with Stage III breast carcinoma.

II. Determine whether this approach will allow for easy surgical intervention without undue complications.

III. Determine whether the sequence of preoperative chemotherapy followed by modified radical mastectomy and an additional 2 years of chemotherapy will change the survival statistics of these patients.

IV. Determine whether preoperative chemotherapy may render some women free of evident disease that might allow for lesser surgeries in the future.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with histologically documented Stage III (UICC classification) breast carcinoma. Patients may not be older than 65 years and must have adequate bone marrow, renal, and hepatic functions. There may be no history of another primary malignancy, myocardial infarction within the past 6 months, or demonstrated coronary artery insufficiency.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893. Methotrexate, MTX, NSC-740 is substituted for ADR after maximum cumulative dose of ADR.

Regimen B: Surgery.

Regimen C: 3-Drug Combination Chemotherapy. CTX; ADR; 5-FU. MTX substitution for ADR.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements, hemogram, estrogen receptor proteins, liver and kidney function tests, EKG, chest x-ray, liver and bone scans, bone survey, skin tests, optional phenocardiogram.

END POINTS: Response/remission rate, duration of response, recurrence rate, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: CTX - 100 mg/sqm/day po on days 1 through 14; ADR - 25 mg/sqm iv on days 1 and 8 (maximum cumulative dose 540 mg/sqm); 5-FU - 500 mg/sqm iv on days 1 and 8. Repeat cycle q 28 days (minimum of 3 courses) until size of breast lesion is stable or until the primary mass has decreased sufficiently to allow for primary closure.

Regimen B: Modified radical mastectomy.

Regimen C: Beginning 2 to 6 weeks postoperatively, resume CTX/ADR/5-FU as in Regimen A. Continue for 2 years, then follow until relapse. After maximum allowable ADR dose has been given, substitute MTX at 40 mg/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

1.0042 COMBINATION CHEMOTHERAPY WITH VBL/MITO FOR ADVANCED REFRACTORY METASTATIC BREAST CARCINOMA

Aisner, J., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America

PROTOCOL NUMBER(S) BCRP-7818

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with vinblastine/mitomycin-c in patients with metastatic breast carcinoma refractory to conventional chemotherapy.

II. Determine the toxicity associated with this combination of agents.

PROTOCOL ENTRY CRITERIA: Patients with disseminated histologically proven carcinoma of the breast who are not candidates for surgery, radiotherapy, or a protocol of higher priority. Patients must have measurable disease and an expected survival of greater than 12 weeks. Previous chemotherapy must have been terminated at least 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Vinblastine, VBL, NSC-49842; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, objective tumor response, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

VBL - 0.15 mg/kg iv on days 1 and 21; MITO - 20 mg/sqm iv on day 1. Repeat q 6 weeks or after recovery from myelosuppression. Continue as long as there is disease stability or evidence of continued response. Patients with progressive disease go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

1.0043 CHEMOTHERAPY WITH ADR/VP-16 FOR ADVANCED RECURRENT ADENOCARCINOMA OF THE BREAST

Van Echo, D. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America

PROTOCOL NUMBER(S) BCRP-7901

OBJECTIVES:

I. Determine the therapeutic efficacy of the combination adriamycin plus VP-16213 in the treatment of advanced recurrent adenocarcinoma of the breast.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven adenocarcinoma of the breast that is not amenable to surgery, radiotherapy, or a higher priority BCRP protocol. Patients must have measurable disease and an expected survival of greater than 8 weeks. There may have been no prior treatment with either of the protocol agents, and all prior chemotherapy and radiotherapy must have ceased at least 4 weeks prior to entry. There may be no prior history of another primary malignant tumor except curatively resected basal cell carcinoma of the skin or surgically cured carcinoma in situ of the cervix.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurement, hemogram, liver and kidney function tests, EKG, chest x-ray, liver and bone scans as indicated, bone survey and bone marrow aspiration as indicated.

END POINTS: Response/remission rate, duration of response, survival, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

ADR - 45 mg/sqm iv on day 1, total cumulative dose not to exceed 540 mg/sqm; VP-16 - 50 mg/sqm iv on days 1 through 5. Repeat course q 21 days or after the recovery of myelosuppression. Give at least 2 courses before declaring failure. Continue treatment as long as disease is stable or there is evidence of continued response. Patients with unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

1.0044 PHASE II CHEMOTHERAPY WITH 5-FU/CTX/PRED WITH OR WITHOUT OOPHORECTOMY FOR ADVANCED BREAST CANCER IN PREMENOPAUSAL WOMEN

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PROTOCOL NUMBER(S) MAYO-763101

OBJECTIVES:

I. Assess the effect of oophorectomy with adjuvant chemotherapy vs. the same chemotherapy without oophorectomy in premenopausal women with advanced breast cancer.

PROTOCOL ENTRY CRITERIA: Premenopausal patients, not previously treated with chemotherapy, with locally recurrent, metastatic or unresectable primary breast cancer beyond surgical or radiotherapeutic control.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy plus Hormone Therapy. CFP: 5-Fluorouracil, 5-FU, NSC-19893; Cyclophosphamide, CTX, NSC-26271; Prednisone, PRED, NSC-10023.

Arm II: Oophorectomy plus 3-Drug Combination Chemotherapy plus Hormone Therapy. 5-FU; CTX; PRED, as in Arm I.

STRATIFICATION BY: Performance status - 0 to 1, or 2 to 3; age - less than 35 years, 35 to 50 years, and more than 50 years; measurable vs. non-measurable disease.

SPECIAL STUDY PARAMETERS: Chest x-ray, metastatic bone survey, estrogens, biological and immune markers.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response, duration of response, duration of progression-free interval, duration of survival, performance status.

CURRENT STATUS: About 25 to 30 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Repeat course q 5 weeks until disease progression. 5-FU - 300 mg/sqm, iv, for days 1 through 5; CTX - 150 mg/sqm, iv, for days 1 through 5; PRED - 30 mg/day, po, for days 1 through 7.

Arm II: Enter patients 3 weeks after oophorectomy. 5-FU; CTX; PRED, asin Arm I.

Follow up all patients for life.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/77

PATIENT ACCRUAL: 00220278

1.0045 CHEMOTHERAPY WITH CAP (CTX/ADR/CACP) VS CFP (CTX/5-FU/PRED) FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) MAYO-783202

OBJECTIVES:

I. Compare the capabilities of CAP: cyclophosphamide (CTX)/adriamycin (ADR)/cis-platinum (CACP) and CFP: CTX/5-fluorouracil (5-FU)/prednisone (PRED) to induce objective regressions in patients with advanced breast cancer.

II. (Addendum 1, February 1979) Develop as secondary treatment for patients progressing on CAP a combination chemotherapy with 5-FU, dibromodulcitol (DBD), plus PRED.

III. Establish a dose schedule with a definite, but tolerable hematologic toxicity defined as: wbc nadir between 1500-2500 cells/cumm and/or PLT nadir between 75,000-100,000 cells/cumm.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed breast cancer with progressive metastatic disease, despite treatment with CAP, that is not amenable to standard surgical or radiotherapeutic techniques.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I or II; enter nonresponders from Arm II to Regimen A (Addendum 1).

Arm I: 2-Drug Combination Chemotherapy plus Hormone Therapy. CFP: 5-Fluorouracil, 5-FU, NSC-19893; Cyclophosphamide, CTX, NSC-26271; Prednisone, PRED, NSC-10023.

Arm II: 3-Drug Combination Chemotherapy. CAP: CTX; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Regimen A: 2-Drug Combination Chemotherapy plus Hormone Therapy. Dibromodulcitol, DBD, NSC-104800; 5-FU; PRED.

STRATIFICATION BY: Performance status: 0-1 vs. 2-3; years post menopause: less than 1 year, 1 to 5 years, 5 to 10 years, over 10 years; dominant disease status: soft tissue vs. osseous vs. visceral.

SPECIAL STUDY PARAMETERS: Estrogen receptor assay, skeletal survey.

END POINTS: Objective tumor response, response rate, duration of regression, interval to progression, survival duration, toxicity/morbidity of treatment.

CURRENT STATUS: 100 patients will be entered.

DOSAGE SCHEDULE:

Arm I: 5-FU - 300 mg/sqm iv on days 1 through 5; CTX - 150 mg/sqm iv on days 1 through 5; PRED - 30 mg/day po on days 1 through 14 (decreasing to 20 mg po on days 15 through 21 and 10 mg po on days 22 through 35). Repeat course q 5 weeks until disease progresses, then remove patient from study.

Arm II: CTX - 400 mg/sqm iv on day 1; ADR - 40 mg/sqm (maximum cumulative dose 500 mg/sqm) iv on day 1; CACP - 40 mg/sqm iv on day 1. Repeat q 4 weeks for 4 courses. Cross over patients to Arm I as soon as progressive disease is observed. Cross over all others to Arm I at completion of 4 courses. (Addendum 1) Enter all patients with disease progression to Arm III.

Regimen A: Enter a minimum of 3 patients to each DBD dosage. DBD - 100 mg/sqm (increasing by 25 mg/sqm for 2 escalations, then by 10% until end point; see Objective III) po on days 1 through 10; plus 5-FU, PRED, as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; CACP - 10 mg vials; DBD - 50 mg tablets; 5-FU and PRED - not given.

DATE SUMMARIZED: 10/78

PATIENT ACCRUAL: 00100379

1.0046 PHASE III CHEMOTHERAPY WITH ADRIAMYCIN (ADR)/DIBROMODULCITOL VS ADR ALONE FOR RESISTANT ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) MAYO-793251

OBJECTIVES:

I. Compare adriamycin (ADR)/dibromodulcitol (DBD) to ADR alone in patients with advanced breast cancer previously exposed to chemotherapy.

II. Obtain Phase II information on DBD as a single agent after ADR failure.

PROTOCOL ENTRY CRITERIA: Postmenopausal patients with measurable or evaluable, histologically confirmed progressive metastatic breast cancer who have failed standard chemotherapy. Patients must have adequate hematologic, renal and hepatic status, and an ECOG performance status better than 4. Patient may not have been exposed to the study agents or similar compounds, and may not have concurrent hormonal therapy for this disease.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arm I or II. Enter patients exiting from ADR therapy to Regimen A.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: 2-Drug Combination Chemotherapy. ADR: Dibromodulcitol, DBD, NSC-104800.

Regimen A: Single-agent Chemotherapy. DBD.

STRATIFICATION: Performance status: 0, 1 vs. 2, 3; dominant disease status: soft tissue vs. osseous vs. visceral; age: under 50 vs. over 50; indicator lesion: measurable vs. evaluable.

SPECIAL STUDY PARAMETERS: Bone survey.

END POINTS: Response/remission rate, objective tumor response, duration of response, time to progression, survival time.

CURRENT STATUS: 125 patients will be entered per year.

DOSAGE SCHEDULE:

Arm I: ADR - 60 mg/sqm (maximum cumulative dose 500 mg/sqm) iv on day 1. Repeat q 28 days until disease progresses or maximum dose is reached.

Arm II: ADR - 40 mg/sqm iv on day 1; DBD - 135 mg/sqm po on days 1 through 10. Repeat course q 28 days until disease progresses or maximum ADR dose reached. Remove from study patients with progressive disease.

Regimen A: Enter patients with disease progression following Arm I therapy and patients from Arm II who have received the maximal ADR dose or who develop cardiac toxicity.

DBD - 180 mg/sqm po on days 1 through 10 q 28 days. Continue until disease progresses then remove patients from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; DBD - 50 mg tablets.

DATE SUMMARIZED: 12/79

1.0047 ENDOCRINE THERAPY WITH AG/TMX/HC VS AG/HC WITH PRIOR TMX VS TMX ALONE FOR BREAST CARCINOMA

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PROTOCOL NUMBER(S) MAYO-803201

OBJECTIVES:

I. Examine the tolerability of the aminoglutethimide (AG), hydrocortisone (HC), and tamoxifen (TMX) regimen.

II. Compare the tolerability and efficacy (regression rates and duration) of the aminoglutethimide/hydrocortisone/tamoxifen regimen with that of tamoxifen alone and aminoglutethimide/hydrocortisone alone.

III. Determine the efficacy of the aminoglutethimide/hydrocortisone regimen in a Phase II fashion in women with prior tamoxifen exposure.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, inoperable, recurrent or metastatic, estrogen receptor status positive or unknown, breast carcinoma, with measurable or evaluable disease. Patients must be postmenopausal, clinically suitable for palliative hormonal therapy and have no known second primary. Patients must have a E.C.O.G. performance status of 3 or better, a serum calcium value less than 12 mg/dl, a serum creatinine value of 1.5 mg/dl or lower and a total bilirubin value less than 2 mg/dl. Patients may receive hormones for medical reasons other than the treatment of breast cancer if the dose is stable, equal to or less than that which is physiologic, and continuous during the protocol therapy. Patients must not have received prior treatment with aminoglutethimide.

PROTOCOL OUTLINE: Patients are randomized to Arms I and II. Those with prior Tamoxifen therapy enter Arm III.

Arm I: Single-agent Hormone Therapy. Tamoxifen, TMX, NSC-180973.

Arm II: 3-Drug Hormone Therapy. Aminoglutethimide, AG, no NSC; plus Hydrocortisone, HC, NSC-10483, plus TMX.

Arm III: 2-Drug Hormone Therapy. AG plus HC.

STRATIFICATION BY: Estrogen receptor status: positive vs. not obtained; performance score (ECOG): 0-1 vs. 2-3; prior hormonal therapy: yes vs. no; prior chemotherapy: yes vs. no.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; tumor measurements; chest x-ray; estrogen receptor; estrogen sulfate; serum dehydroepiandrosterone sulfate; thyroxine; metastatic bone survey.

END POINTS: Response/remission rate, duration of regression, objective tumor response, length of survival, disease-free interval.

CURRENT STATUS: Study is expected to accrue 100 patients per year.

DOSAGE SCHEDULE:

Arm I: TMX - 10 mg po daily.

Arm II: TMX - 20 mg in 2 equal doses po daily; AG - 500 mg in 2 equal doses po daily; HC - 100 mg po daily (at 8 AM 20 mg, at 2 PM 20 mg, at 5 PM 60 mg) on days 1 to 15; beyond day 15, HC - 40 mg po daily (at 8 AM 10 mg, at 5 PM 10 mg, at bedtime 20 mg).

Arm III: AG - 1000 mg in 4 equal doses po daily; HC - 100 mg po daily (at 8 AM 20 mg, at 2 PM 20 mg, at 5 PM 60 mg) on days 1 to 15; beyond day 15, HC - 40 mg po daily as per Arm II.

Patients are assessed at one month and q 2 months thereafter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - 10 mg tablets; HC - 10 and 20 mg tablets; AG - 250 mg tablets.

DATE SUMMARIZED: 08/80

1.0048 CHEMOTHERAPY WITH CMF (CYCLOPHOSPHAMIDE/METHOTREXATE/5-FLUOROURACIL) AND IMMUNOTHERAPY WITH BCG FOR STAGE I BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-209; MDA-MBDT-7718

OBJECTIVES:

I. Evaluate the efficacy of CMF chemotherapy in combination with nonspecific BCG immunotherapy for the prolongation of disease-free survival and for the prevention of metastatic disease in Stage I breast carcinoma.

II. Evaluate and monitor short- and long-term complications and toxicity from the proposed regimen.

III. Evaluate biological markers as aids for monitoring adjuvant therapy.

IV. Evaluate immunocompetence by skin tests with recall antigens during radiotherapy and chemoimmunotherapy as predictive of prognosis.

PROTOCOL ENTRY CRITERIA: Patients under 65 years of age with carcinoma of the breast, UICC Stage T1, T2, N0, M0, with primary tumor no more than 5 cm in greatest dimension and no evidence of palpable or biopsy-positive axillary nodes or distant metastasis. Primary regional therapy must have been carried out within 3 months prior to entry. Patient must have adequate renal and liver function, and be psychologically stable.

PROTOCOL OUTLINE: Nonrandomized study. Compare results with response to other therapies in historical controls.

3-Drug Combination Chemotherapy plus Immunotherapy. CMF: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; plus BCG-Connaught, BCG, NSC-B116341.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, disease-free interval, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: 200 patients will be entered over 2 years.

DOSAGE SCHEDULE:

CMF: CTX - 100 mg/sqm iv on day 1; MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8. Repeat course q 28 days for a minimum of 2 courses. BCG - 6 x 10 to the 8th organisms by scarification on days 9, 16 and 23. Continue BCG twice monthly for 3 months following completion of Chemotherapy.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/77

1.0049 RADIOTHERAPY PLUS CHEMOTHERAPY WITH DIBROMODULCITOL/FTORAFUR/ADR FOR BREAST CARCINOMA METASTATIC TO BRAIN

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PROTOCOL NUMBER(S) MDAR-233; MDA-MBDT-7736

OBJECTIVES:

I. Attempt to increase survival of patients with brain metastases from breast carcinoma by radiotherapy plus chemotherapy with adriamycin (ADR)/dibromodulcitol/ftorafur.

II. Attempt to increase response and survival in patients with predominant brain metastases using more aggressive radiotherapy than usual.

III. Compare the efficacy of different radiation doses and techniques of administration for brain metastases.

PROTOCOL ENTRY CRITERIA: Patients with histologically-proven breast cancer plus clinical evidence of brain metastases who have not had prior treatment with ftorafur or dibromodulcitol or whole brain radiation.

PROTOCOL OUTLINE: Randomized study for patients in Group I only. Randomize Group I patients (minimal or absent extracranial metastases) to Arms I or II. Enter Group II patients (significant brain and extracranial metastases) to Regimen A. Enter Group III patients (recurrent brain metastases maximally treated by Radiotherapy and Surgery) to Regimen B.

Arm I: Radiotherapy followed by 3-Drug Combination Chemotherapy. Aggressive Radiotherapy followed by Adriamycin, ADR, NSC-123127 or Methotrexate, MTX, NSC-740; Ftorafur, NSC-148958; Dibromodulcitol, DBD, NSC-104800.

Arm II: Radiotherapy followed by 3-Drug Combination Chemotherapy. Radiotherapy - different schedule from Arm I, followed by ADR, Ftorafur, DBD.

Regimen A: Radiotherapy plus 3-Drug Combination Chemotherapy. Palliative Radiotherapy plus ADR; Ftorafur; DBD.

Regimen B: Single-agent Chemotherapy. DBD.

STRATIFICATION BY: Minimal vs. significant extracranial metastases.

SPECIAL STUDY PARAMETERS: EEG, brain scan; computerized axial tomography; liver, spleen and bone scans; cerebral arteriogram, skin tests for recall antigens.

END POINTS: Objective tumor response, response/remission rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: About 60 patients will be entered.

DOSAGE SCHEDULE:

Arm I: 5000 rads in 5 weeks to the whole brain. Give patients with a solitary metastasis 4000 rads to the whole brain in 4 weeks followed by 1000 rads boost to metastasis in the last week. Give patients with multiple metastases 5000 rads in 5 weeks to the whole brain; followed, for patients without previous drug exposure, by ADR -50 mg/sqm iv on day 1 (total maximum dose 450 mg/sqm); Ftorafur - 4 gms/sqm iv on day 1; DBD - 80 mg/sqm po on days 1 through 5. Repeat course q 21 days. After maximum dose of ADR is reached, substitute MTX - 50 mg/sqm iv or im. If patient has had extensive prior exposure to ADR: MTX - on day 1 only; Ftorafur - on day 1 only; DBD - on days 1 through 5. Repeat only DBD q 21 days. If patient has had extensive prior exposure to both ADR and MTX: Ftorafur on day 1 only; DBD on days 1 through 10 and beginning again on day 22.

Arm II: 4500 rads in 10 days to whole brain; followed by: ADR; Ftorafur; DBD, as in Arm I.

Regimen A: 3000 rads in 10 days to whole brain; plus concurrent ADR; Ftorafur; DBD, as in Arm I:

Regimen B: DBD - 125 mg/sqm po on days 1 through 14 q 21 days. Escalate dose to tolerance.

All patients receive corticosteroids or glycerol during Radiotherapy and for 1 to 3 weeks afterwards. Remove from study patients with disease progression after Radiotherapy and 2 courses of Chemotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Ftorafur - 500 mg vials; ADR - 10 mg ampules; DBD -25 mg tablets; MTX - 5 and 50 mg vials.

DATE SUMMARIZED: 09/79

PATIENT ACCRUAL: 00620979

1.0050 CHEMOTHERAPY WITH FAC (5-FU/ADR/CTX) PLUS MER IMMUNOTHERAPY FOLLOWING REGIONAL RADIOTHERAPY FOR RECURRENT BREAST CARCINOMA

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PROTOCOL NUMBER(S) MDAR-237; MDA-MBDT-7749

OBJECTIVES:

I. Determine the efficacy of the combination FAC-BCG: 5-fluorouracil (5-FU), adriamycin (ADR), cyclophosphamide (CTX) and BCG as adjuvant therapy for Stage IV NED breast cancer following regional therapy with radiation and/or surgery for isolated recurrence.

II. Determine the qualitative and quantitative toxicity of 5-FU, ADR, CTX and BCG.

PROTOCOL ENTRY CRITERIA: Patients under 75 years old with histologically confirmed, isolated resectable recurrence of carcinoma of the breast (local, regional, or distant) who have no evidence of metastatic disease. Patients must not have had prior chemotherapy with alkylating agents.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Immunotherapy. FAC-BCG: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; plus BCG, type not specified. When the maximum cumulative dose of ADR has been reached, change to CMF-BCG, substituting Methotrexate, MTX, NSC-740 for ADR.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Toxicity/morbidity of treatment, recurrence rate, appearance of metastases.

CURRENT STATUS: About 50-60 patients will be entered in one year.

DOSAGE SCHEDULE: 5-FU - 500 mg/sqm iv on days 1 and 8; ADR - 50 mg/sqm iv on day 1 (maximum cumulative dose 450 mg/sqm); CTX - 500 mg/sqm iv on day 1; BCG - by scarification on days 9, 13, and 17. Repeat cycle q 22 days. When ADR has been administered to the maximum cumulative dose, substitute: MTX - 30 mg/sqm im on days 1 and 8. Continue therapy for a total of 2 years, then maintain patient on BCG only q 14 days for 6 months. Remove any patient from study who shows evidence of metastases.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

1.0051 HIGH DOSE VS STANDARD COMBINATION CHEMOTHERAPY WITH 5-FU/ADR/CTX AND 5-FU/MTX/CTX FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-259; MDA-MBDT-7807

OBJECTIVES: (This protocol replaces MDAR-150.)

I. Determine whether higher doses of chemotherapy with 5-fluorouracil (5-FU)/adriamycin (ADR)/cyclophosphamide (CTX) result in higher response rates, longer duration of response, and longer duration of survival.

PROTOCOL ENTRY CRITERIA: Patients with previously untreated histologically proven Stage III breast cancer. Patients must have adequate bone marrow, renal and liver function and be under 65 years of age.

PROTOCOL OUTLINE: Randomized study. Following treatment on Arm I or Arm II, patients enter Maintenance.

Arm I: 3-Drug Combination Chemotherapy plus protective environment prophylactic antibiotic therapy. 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm II: 3-Drug Combination Chemotherapy. 5-FU; ADR; CTX.

Maintenance: 3-Drug Combination Chemotherapy. 5-FU; CTX; Methotrexate, MTX, NSC-740.

STRATIFICATION BY: Estrogen receptor status, dominant site of disease, menopausal status.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, duration of response, duration of survival.

CURRENT STATUS: About 30 evaluable patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Arm I: 5-FU - 500 mg/sqm iv on days 1 through 5; ADR - 70 mg/sqm (increase to 85 mg/sqm then 100 mg/sqm in second and third courses; maximum cumulative dose 450 mg/sqm) iv on day 1; CTX - 1200 mg/sqm (increase to 1500 mg/sqm then 1800 mg/sqm in second and third courses). Therapy is given in a protective environment unit. Give subsequent course when patient has recovered from myelosuppressive activity of treatment. Continue therapy until the maximum ADR dose is reached, then enter patient to Maintenance.

Arm II: 5-FU - 500 mg/sqm iv on days 1 and 8; ADR - 50 mg/sqm iv on day 1; CTX - 500 mg/sqm iv on day 1. Repeat course q 3 weeks or when patient has recovered from myelosuppressive activity of treatment. Continue therapy until maximum ADR dose is reached, then enter patient to Maintenance.

Maintenance: 5-FU - 600 mg/sqm iv on days 1 and 8; MTX - 50 mg/sqm iv on days 1 and 8; CTX - 600 mg/sqm if on day 1. Repeat course q 4 weeks and continue therapy for 2 years for patients who remain in continuous remission.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

1.0052 CHEMOTHERAPY WITH FAC (5-FU/ADR/CTX) WITH OR WITHOUT INTERFERON IMMUNOTHERAPY FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-295; MDA-DT-7827

OBJECTIVES:

I. Determine whether the addition of leukocyte interferon to combination chemotherapy with 5-fluorouracil (5-FU), adriamycin (ADR), and cyclophosphamide (CTX) will increase the complete remission rate, remission duration, and prolong the survival of patients with metastatic breast cancer.

II. Determine the effects of chemotherapy on the pharmacology and immunological effects of interferon.

III. Determine whether interferon reduces the incidence of infection in patients receiving combination chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with measurable and histologically proven metastatic unresectable breast carcinoma not refractory to 5-FU, methotrexate or ADR. Patients must have adequate bone marrow and renal function, be off all prior therapy for three weeks, and be free of CNS metastases.

PROTOCOL OUTLINE: Randomized study.

Arm I:

Induction: 3-Drug Combination Chemotherapy. FAC: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Maintenance: 3-Drug Combination Chemotherapy. CMF: CTX; Methotrexate, MTX, NSC-740; 5-FU.

Arm II:

Induction: 3-Drug Combination Chemotherapy plus Immunotherapy. FAC plus Interferon.

Maintenance: 3-Drug Combination Chemotherapy plus Immunotherapy. CMF plus Interferon.

STRATIFICATION BY: Pre- vs. post-menopausal, number of organ sites involved, dominant tumor sites.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, duration of response, length of survival, toxicity/morbidity of treatment, immunocompetence, objective tumor response.

CURRENT STATUS: 110 patients will be entered in about 6 months.

DOSAGE SCHEDULE:

Arm I:

Induction: FAC: 5-FU - 500 mg/sqm iv on days 1 and 8; ADR - 50 mg/sqm iv on day 1; CTX - 500 mg/sqm iv on day 1. Repeat course q 21 days.

Maintenance: CMF: Discontinue ADR after a total dose of 500 mg/sqm and maintain patients on MTX - 50 mg/sqm iv or im on days 1 and 8; CTX - 600 mg/sqm iv on day 1; 5-FU - 600 mg/sqm on days 1 and 8. Repeat course q 21 days.

Arm II:

Induction: FAC as in Arm I; Interferon - 3 million units/day im on days 5 through 14.

Maintenance: CMF as in Arm I; Interferon - 3 million units 1 day im (or sc if the platelet count is less than 50,000/cu mm) on days 5 through 14. Repeat course q 21 days.

Give a minimum of two 21-day courses of Arm I or Arm II for an adequate trial.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/79

1.0053 FAC FOLLOWED BY CMF COMBINATION CHEMOTHERAPY AND BCG ALONE VS BCG PLUS IRRADIATED ALLOGENEIC CANCER CELLS FOR INFLAMMATORY BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-309; MDA-MBDT-7861

OBJECTIVES:

I. Institute an intensive cytoreductive combined modality program of Induction chemotherapy with FAC - 5-Fluorouracil (5-FU)/Adriamycin (ADR)/Cyclophosphamide (CTX) and Maintenance chemotherapy with CMF -CTX/Methotrexate (MTX)/5-FU for inflammatory breast cancer.

II. Evaluate toxicity and feasibility of active specific immunotherapy of repeated injections of BCG alone or in combination with irradiated allogeneic cultured breast cancer cells.

III. Evaluate specific and nonspecific in vitro and in vivo immune response as correlates of immunotherapy and as related to such clinical features as response, duration of remission, and survival.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with clinically diagnosed inflammatory breast cancer without metastases except regional lymphadenopathy. Mastectomy prior to presentation at MDAH must have been performed no more than one month prior to start of present therapy. Patients must have adequate renal and bone marrow function, and must not be taking steroids.

PROTOCOL OUTLINE: Randomized study for Immunotherapy only.

Induction:

3-Drug Combination Chemotherapy followed by Debulking Surgery if indicated. FAC: 5-Fluorouracil, 5-FU, NSC-19593; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Immunotherapy: Randomize patients to Arm I or Arm II.

Arm I: Immunotherapy. BCG.

Arm II: Combination Immunotherapy. BCG plus tumor cells.

Maintenance: Enter all patients.

3-Drug Combination Chemotherapy. CMF: CTX; Methotrexate, MTX, NSC-740; 5-FU. Following Maintenance, repeat Immunotherapy, Arm I or Arm II, followed by Radiotherapy, unless earlier radiation treatments were provided for local treatment.

STRATIFICATION BY: Menopausal status, time of prior surgery.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, disease-free interval, survival rate.

CURRENT STATUS: 42 patients will be entered.

DOSAGE SCHEDULE:

Induction: Enter all patients within 4 weeks of mastectomy. FAC: 5-FU - 500 mg/sqm iv on days 1 and 8; ADR - 50 mg/sqm iv on day 1; CTX -500 mg/sqm iv on day 1. Repeat course q 21 days for 3 courses. Perform Debulking Surgery if indicated.

Immunotherapy: Begin 3 weeks after start of third Induction course. Randomize patients to Arms I or II.

Arm I: BCG plus Tumor Cell Mixture (irradiated allogeneic breast cancer cells) - 2.0 ml in 10 divided doses id over scapula contralateral to the affected breast. Repeat after 7 days into upper thigh.

Arm II: BCG alone, id as in Arm I. Rest two weeks.

Maintenance:

CMF: CTX - 600 mg/sqm iv on day 1; MTX - 50 mg/sqm iv or im on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8. Repeat course q 21 days. Repeat Arm I or Arm II Immunotherapy at conclusion of Maintenance, 2 years after start of Chemotherapy.

Enter patients for Debulking Surgery after 2 to 4 courses of Induction Chemotherapy, as indicated. Enter patients to Radiotherapy (no dosages given) after last courses of Immunotherapy unless radiation has been employed for early or appropriate localized treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/79

1.0054 TMX, CTX/5-FU/ADR OR MTX, PSEUDOMONAS VACCINE & SURGICAL DEBULKING & RADIATION CONSOLIDATION FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-351; MDA-DT-7937

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with 5-fluorouracil (5-FU)/adriamycin (ADR)/cyclophosphamide (CTX) plus hormone therapy with tamoxifen (TMX) with and without pseudomonas vaccine immunotherapy for metastatic breast cancer.

II. Determine the feasibility of surgical tumor reduction without interfering with systemic therapy, and its effect on duration of remission and survival.

III. Determine the feasibility of simultaneous chemotherapy and radiotherapy.

IV. Determine toxicity of this regimen.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable or evaluable progressive metastatic breast tumor who are not eligible for the PEPA study. Patients must have adequate cardiac status and bone marrow function unless inadequacy is secondary to tumor replacement. Patients must not have had radiation or chemotherapy in prior 3 weeks. They may not have central nervous system metastases or resistance to protocol drugs.

PROTOCOL OUTLINE: Randomized study for Immunotherapy. Patients with estrogen-receptor-positive (ER positive) or unknown (ER?) status enter Regimen A. After initial therapy on Regimen A, these patients and all other patients are randomized to Arms I and II. All patients proceed to Regimen C and then responders proceed to Regimen D.

Regimen A: Single-agent Hormone Therapy. Tamoxifen, TMX, NSC-180973.

Arm I:

Induction: 3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

Maintenance: 3-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; 5-FU, CTX.

Arm II:

Induction: 3-Drug Combination Chemotherapy plus Immunotherapy. 5-FU; CTX; ADR; plus Pseudomonas vaccine.

Maintenance: 3-Drug Combination Chemotherapy plus Immunotherapy. MTX; 5-FU; CTX; plus Pseudomonas vaccine.

Regimen B: Surgery. Debulking procedures.

Regimen C: Consolidation. Radiotherapy.

STRATIFICATION: Number of metastatic sites, performance status, immunocompetence, estrogen receptor status.

SPECIAL STUDY PARAMETERS: CEA; bone and liver scans; mammogram; immunological evaluation including skin tests for recall antigens; serum lysozyme levels and immune complexes.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: About 120 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Regimen A: TMX - 20 mg/day po in 2 divided doses for 6 to 8 weeks, then evaluate patients. Patients with progressive disease discontinue TMX and enter Induction and Maintenance. Patients with stable or improved disease status enter Induction and Maintenance and continue TMX. Patients with life-threatening disease begin Regimen A and Induction and Maintenance concurrently.

Arm I: Induction. 5-FU - 500 mg/sqm iv on day 1 and 8; CTX - 500 mg/sqm iv on day 1; ADR - 50 mg/sqm (maximum dose 450 mg/sqm) iv on day 1.

Repeat course q 21 days, escalating dosages to 600 mg/sqm for 5-FU, CTX and to 60 mg/sqm for ADR, if hematologic toxicity permits.

Maintenance: When total maximum dose of ADR has been reached, substitute MTX - 50 mg/sqm im on days 1 and 8 followed 2 hours later by 5-FU, CTX, as in Induction, using 600 mg/sqm dosages. If toxicity permits, escalate dosages to 700 mg/sqm for 5-FU and CTX, and to 60 mg/sqm for MTX.

Arm II: Induction and Maintenance as in Arm I; plus Pseudomonas vaccine - 0.25 mg/sqm sc rotating to upper arms and thighs on days 8 and 16 of each Induction or Maintenance course.

Regimen B: Restage all patients after 6 courses of Arm I or Arm II Induction, with maximal surgical removal of residual tumor, resection of metastatic lesions and treatment of pleural effusions and intrahepatic lesions.

Regimen C: Enter patients achieving complete response on Maintenance, preferably after 1 year of systemic therapy. Give 5000 to 6000 rads in 3 to 4 weeks to local chest wall disease, and the same dosage to regional recurrence involved fields in 4 to 5 weeks, and 3000 to 4000 rads in 2 to 3 weeks to distant metastases.

Continue systemic therapy Regimen A and Arm I or II for patients with stable disease or PR until relapse. For patients who achieve CR continue therapy for at least 2 years after start of therapy of 1 year after reaching CR, whichever is longer.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

1.0055 COMBINATION CHEMOTHERAPY WITH VBL/ADR FOR METASTATIC BREAST CANCER REFRACTORY TO CMF (CTX/MTX/5-FU)

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PROTOCOL NUMBER(S) MDAR-353; MDA-MBDT-7933

OBJECTIVES:

I. Determine the antitumor activity of continuous infusion of vinblastine plus adriamycin in Stage IV breast cancer patients who have shown progression on combination chemotherapy with CMF (cyclophosphamide/methothrexate/5-FU).

II. Define qualitative and quantitative toxicity of this regimen.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven breast cancer who developed metastatic disease on CMF regimen. Patients who have had prior ADR or other anthracyclines are excluded. Prior exposure to conventional dose schedule of vinca alkaloids is acceptable. Life expectancy must be at least 8 weeks with Karnofsky performance status of more than 30 percent. Patients must be off all prior chemotherapy for at least 3 weeks and fully recovered from their toxicity; they should be off hormone therapy at least 4 weeks. Measurable lesions must be present.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Vinblastine, VBL, NSC-49842; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Prior chemotherapy, disease stage.

SPECIAL STUDY PARAMETERS: SMA-100; CEA; bone, brain and liver scan; x-ray of abnormal bone; EKG and recording of sum of voltages of QRS complexes; full cardiological evaluation when indicated; endocrinal biopsy.

END POINTS: Response/remission, partial remission, toxicity.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

VBL - 1.2 mg/sqm as a continuous iv 24-hour infusion days 1 to 4; at completion of VBL, start ADR - 40 mg/sqm over 48 hours. Give both drugs via central venous catheter or pump. Repeat courses q 21 to 28 days provided patient has recovered from myelosuppression of the previous cycle.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

1.0056 ENDOCRINE THERAPY WITH AMINOGLUTETHIMIDE FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-366; MDA-MBDT-7959

OBJECTIVES:

I. Determine the therapeutic efficacy of aminoglutethimide in advanced breast cancer patients with prior response to tamoxifen therapy.

II. Determine the qualitative and quantitative toxicity of the drug.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven breast cancer who have developed progressive metastatic disease after initial response to tamoxifen will be entered. Patients must have an objective regression of tumor on tamoxifen therapy and have a positive estrogen receptor after failing tamoxifen therapy. Toxic effects from prior hormonal and chemotherapy must not be evident and lesions must be measurable. Patients with CNS metastases are not eligible and bone marrow function should be adequate. Life expectancy of at least 8 weeks and a Karnofsky performance status of more than 30 are required.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Endocrine Therapy. Aminoglutethimide, AGT, no NSC number.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Radioisotopic studies.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 50-60 evaluable patients will be entered to determine a 30-40 percent response to drug.

DOSAGE SCHEDULE:

AGT - 1000 mg/day in 4 divided doses po. Development of fever, rash, lethargy, nausea, ataxia, nystagmus, or dizziness leads to temporary reduction to 500 mg/day in 2 divided doses until symptoms abate, upon which dosage is returned to 1000 mg/day.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AGT - 250 mg tablets.

DATE SUMMARIZED: 05/80

1.0057 PHASE II STUDY OF CONTINUOUS VS INTERMITTENT DOSES OF VP-16213 FOR PATIENTS WITH REFRACTORY METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-372; MDA-DT-7984

OBJECTIVES:

I. Compare the therapeutic efficacy in terms of response rate and survival of continuous 5-day infusion VP-16213 versus intermittent bolus doses daily for 5 days in patients with metastatic breast cancer who have failed higher priority protocols.

II. Determine the qualitative and quantitative toxicity of these dose schedules.

PROTOCOL ENTRY CRITERIA: All patients with metastatic breast cancer who have failed on protocols of higher priorities and without prior exposure to podophyllotoxins are eligible. All patients must have a life expectancy of at least 8 weeks and a Karnofsky performance status of more than 30 percent. Patients should have been off all prior chemotherapy for at least six weeks prior to entry. Patients should have measurable lesions.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. VP-16213, VP-16, NSC-141540. Continuous infusion.

Arm II: Single-agent Chemotherapy, VP-16. Intermittent bolus.

STRATIFICATION BY: Prognostic risk: good (adequate bone marrow reserve and normal liver function) vs. poor.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, objective tumor response, disease-free interval.

CURRENT STATUS: A 25 patient minimum is required for each arm. Additional patients will be entered if response rates on each arm are in excess of 20 percent, or if statistical considerations justify it.

DOSAGE SCHEDULE:

Arm I: Good risk patients: VP-16 - 15 mg q 6 hours as continuous 24-hour infusion daily for 5 days. Infusion given via central venous catheter. Course repeated q 3 weeks. Poor risk patients: 50 mg/sqm daily for 5 days. Dosage increased or decreased on basis of granulocyte and platelet counts at end of previous course.

Arm II: VP-16 - 60 mg/sqm iv bolus daily for 5 days. Details as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

1.0058 PHASE I-II ENDOCRINE THERAPY WITH TRIOXIFENE MESYLATE FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-375; MDA-DT-7991

OBJECTIVES:

I. Determine the antitumor activity and toxicity of trioxifene in patients with metastatic breast cancer.

II. Determine the relationship of dose of trioxifene to its antitumor activity and toxicity.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented breast cancer with clinical evidence of recurrence and measurable disease. Patients unresponsive to previous antiestrogens are not eligible. Patients must be fully ambulatory and have a life expectancy of at least 3 months. Patients must have adequate renal and hematologic function. Patients must receive no chemotherapy within the 3 weeks prior to entry; they must have fully recovered from any toxic effects.

PROTOCOL OUTLINE: Patients will be allocated to one of three dose levels.

Single-agent Antiestrogen Therapy. Trioxifene mesylate, Trioxifene.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, objective tumor response, duration of response.

CURRENT STATUS: 75 evaluable patients will be entered during a 12-month period.

DOSAGE SCHEDULE:

Patients are treated at one of three dose levels.

Trioxifene - 10 mg in 2 equally divided doses daily or 20 mg in 2 equally divided doses daily or 40 mg in 2 equally divided doses daily. Treatment is continued for a minimum of 4 weeks, preferably 6 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/80

1.0059 PHASE II COMBINATION CHEMOTHERAPY WITH AMSA/VBL FOR METASTATIC BREAST CANCER REFRACTORY TO FAC-CMF CHEMOTHERAPY

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PROTOCOL NUMBER(S) MDAR-389; MDA-MBDT-8009

OBJECTIVES:

I. Determine response rate and duration of response to the combination of m-AMSA and vinblastine in patients with metastatic breast cancer refractory to FAC-CMF chemotherapy.

II. Determine the qualitative and quantitative toxicity of this drug combination.

PROTOCOL ENTRY CRITERIA: Patients with metastatic breast cancer with measurable lesions who have failed chemotherapy with FAC-CMF. Patients must not have received any other chemotherapy. Patients must be ambulatory, have a performance score greater than 30 percent, and have normal renal and hepatic function. Patients must have no brain metastasis or spinal cord compression and have received no chemotherapy or hormones for 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. m-AMSA, AMSA, NSC-249992; Vinblastine, VBL, NSC-49842.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Remission/response rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Initially 25 patients will be entered; if the response rate is greater than 20 percent, more patients will be entered.

DOSAGE SCHEDULE:

VBL - 2 mg/sqm iv on days 1 to 3; AMSA - 20 mg/sqm iv on days 1 to 3. Course is repeated at 21-day intervals provided patient has recovered from myelosuppression. Patients receive at least 2 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/80

1.0060 PHASE II CHEMOTHERAPY WITH AZQ FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-394; MDA-MBDT-8020

OBJECTIVES:

I. Determine the efficacy of AZQ administered by intravenous 5-day intermittent schedule to patients with breast cancer.

II. Determine the qualitative and quantitative toxicity of AZQ administered in this fashion.

III. Determine duration of response and survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic breast cancer with measurable lesions who are not candidates for known regimens or higher priority protocol treatments. Patients with brain metastases or meningeal carcinomatosis are not excluded. Patients must have a life expectancy of at least 12 weeks and adequate bone marrow function. Patients must not have received chemotherapy, immunotherapy, or radiotherapy for 4 weeks prior to entry and must have recovered from any toxic effects of previous therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. AZQ, NSC-182986.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic function tests.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, survival rate, length of survival, objective tumor response.

CURRENT STATUS: 25-30 patients will be entered, unless all first 14 patients entered fail to respond.

DOSAGE SCHEDULE:

AZQ - 8 mg/sqm (good-risk patients, with bilirubin less than 2 mg percent and adequate bone marrow reserve) iv daily for 5 days q 28 days. Poor-risk patients (bilirubin between 2 mg and 5 mg percent and poor bone marrow reserve) receive 6 mg/sqm. Dose is increased by 25 percent for the second course and by 50 percent for the third course if granulocyte and platelet counts are adequate. All patients receive at least 2 courses of therapy. Chemotherapy is continued for 2 years or for 1 year after CR, whichever is shorter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/80

BREAST TUMORS

1.0061 PHASE II CHEMOTHERAPY WITH CARMINOMYCIN FOR REFRACTORY STAGE IV BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-404; MDA-MBDT-8030

OBJECTIVES:

I. Determine the antitumor activity of carminomycin in patients with metastatic breast cancer who have failed prior non-anthracycline combination chemotherapy such as CMF.

II. Determine the qualitative and quantitative toxicity of carminomycin given on a single iv intermittent schedule.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven breast cancer who have failed all front-line chemotherapy and who have objective evidence of progressive disease with measurable lesions or who have developed metastatic disease following adjuvant chemotherapy. Patients must have a life expectancy of at least 12 weeks and have adequate renal function and normal liver function. Patients must have no evidence of cardiac failure, clinically significant arrythmias or a history of myocardio infarction within the previous six months. Patients must receive no hormone therapy for at least 6 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study. All patients enter Regimen A. Patients with progressive disease after 2 courses or no response after 4 courses change to Regimen B.

Regimen A: Single-agent Chemotherapy. Carminomycin, CMM, NSC-180024.

Regimen B: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Granulocyte and platelet counts.

END POINTS: Response/remission rate, objective tumor response.

CURRENT STATUS: 25-30 patients will be entered, unless all of the first 14 patients fail to respond.

DOSAGE SCHEDULE:

Regimen A: CMM - 20 mg/sqm iv push q 3 weeks. Patients with progressive disease after 2 courses or who show no response after 4 courses change to Regimen B.

Regimen B: ADR - 60 mg/sqm iv push q 3 weeks.

All responding patients continue on study until evidence of progression and/or development of unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

1.0062 FACVP (5-FU/ADR/CTX/VCR/PRED) PLUS MAINTENANCE WITH TMX VS TMX/MTX/VBL VS MTX/VBL FOR STAGE II, III BREAST CARCINOMA

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PROTOCOL NUMBER(S) MDAR-408; MDA-MBDT-8026

OBJECTIVES:

I. Determine the effect of the addition of vincristine and prednisone to adjuvant FAC (5-fluorouracil/adriamycin/cyclophosphamide) chemotherapy on disease-free interval and survival for Stage II, III breast cancer.

II. Determine whether Maintenance therapy with tamoxifen alone, tamoxifen with methotrexate/vinblastine or with methotrexate/vinblastine (estrogen-receptor-positive patients) alone improves the result.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven carcinoma of the breast with one or more positive nodes, who are free of systemic disease on complete staging. Patients must be under 75 years of age and must not have been previously treated with any of the protocol agents.

PROTOCOL OUTLINE: Study randomized for Maintenance only. Estrogen-receptor-negative patients enter Regimen A and proceed to Regimen B Maintenance. Estrogen-receptor-positive patients enter Regimen A and are then randomized to Arms I and II for Maintenance.

Regimen A: 4-Drug Combination Chemotherapy and Hormone Therapy. FACVP: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Maintenance:

Regimen B: 2-Drug Sequential Chemotherapy. Methotrexate, MTX, NSC-740; Vinblastine, VBL, NSC-49842.

Arm I: Hormone Therapy. Tamoxifen, TMX, NSC-180973.

Arm II: 2-Drug Sequential Chemotherapy plus Hormone Therapy. MTX; VBL; plus TMX.

STRATIFICATION BY: Estrogen receptor status: positive vs. negative vs. unknown; menopausal status: pre vs. post; disease stage: II vs. III; prior postoperative radiotherapy: yes vs. no.

SPECIAL STUDY PARAMETERS: Granulocyte and platelet counts, EKG.

END POINTS: Disease-free interval, survival.

CURRENT STATUS: About 200 evaluable patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Chemotherapy is initiated within 2-3 weeks after Surgery and is given in a 21-day cycle. FACVP: VCR - 0.25 mg/sqm iv (maximum total dose 2 mg) on day 1; ADR - 50 mg/sqm iv on day 1 (ADR total dose is limited to 300 mg/sqm for estrogen-receptor-positive patients, patients with 1-3 positive nodes, and T2N0 and T3N0 patients; for all other patients, total ADR dose is 400 mg/sqm); CTX - 500 mg/sqm iv on day 1; 5-FU - 500 mg/sqm iv on days 1 and 8; PRED - 40 mg po on days 1 through 5. Repeat cycle q 21 days.

Maintenance:

Regimen B: MTX - 75 mg/sqm iv q 2 weeks for 6 doses; beginning after the completion of 6 MTX doses, VBL - 1.7 mg/sqm iv on days 1 through 5 q 3 weeks for 4 cycles.

Arm I: TMX (no dosage or schedule details given).

Arm II: TMX (no details given); plus MTX and VBL as in Regimen B.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

1.0063 PHASE II IMMUNOTHERAPY WITH POLY ICLC FOR REFRACTORY METASTATIC BREAST CANCER

Hortobagyi, G. N., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-413; MDA-MBDT-8027

OBJECTIVES:

I. Evaluate the interferon-inducing ability of poly-ICLC in patients with metastatic breast cancer.

II. Evaluate the therapeutic efficacy of poly-ICLC or the interferon produced by this agent in patients with metastatic breast cancer.

III. Evaluate the quantitative and qualitative toxicity of poly-ICLC.

IV. Evaluate host defense modulation by poly-ICLC.

PROTOCOL ENTRY CRITERIA: Patients with clearly measurable and progressive metastatic breast cancer who have failed all known effective chemotherapy and hormone therapy programs. Patients must not have brain metastases or spinal cord compression. Patients must have normal renal function, must be off all chemotherapy and hormone therapy for the 3-week period prior to entry, and must be fully recovered from any resultant toxicity. No simultaneous treatment with chemotherapy or hormone therapy will be allowed.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy. Poly-ICLC, Poly-IC, NSC-120949.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, objective tumor response, duration of remission, disease-free interval.

CURRENT STATUS: A minimum of 15 evaluable patients will be required.

DOSAGE SCHEDULE:

Poly-IC - 4 mg/sqm iv over 4 hours, repeated weekly. A minimum of 4 weeks of treatment is required for an adequate trial; therapy is continued until evidence of progressive disease is observed.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

1.0064 PHASE II CHEMOTHERAPY WITH HEPATIC ARTERIAL INFUSION OF VBL FOR METASTATIC CARCINOMA OF THE BREAST CONFINED TO THE LIVER

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PROTOCOL NUMBER(S) MDAR-419; MDA-MBDT-8046

OBJECTIVES:

I. Determine the feasibility of continuous arterial infusion of vinblastine to patients with metastatic carcinoma of the breast regionally confined to the liver.

II. Determine the response rate, duration of response, and survival of patients treated by hepatic arterial infusion (HAI) of vinblastine for metastatic carcinoma of the breast regionally confined to the liver.

III. Compare the pharmacology of continuous intravenous administration and continuous HAI of vinblastine given to patients with metastatic breast cancer.

IV. Consider this therapy for Consolidation of breast cancer metastatic to the liver.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven primary carcinoma of the breast, and with breast cancer with metastatic disease primarily confined to the liver, who are not candidates for higher priority protocols. Disease in the liver should be measurable by one of the imaging techniques (radionuclide scan, ultrasound or CT scan of the liver, or angiography). Patients must have a life expectancy of at least 12 weeks and there must be adequate bone marrow reserve. Special provision will be made for patients with severely deranged liver functions. Patients must not have received prior Vinca alkaloid chemotherapy. All chemotherapy, radiotherapy, or immunotherapy must have been withdrawn at least 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vinblastine, VBL, NSC-49842.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic and hepatic function tests, tumor measurements.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response.

CURRENT STATUS: An accrual of 15 to 20 evaluable patients is necessary.

DOSAGE SCHEDULE:

VBL - 2.0 mg/sqm continuous hepatic arterial infusion over 24 hours for 5 days q 3 weeks. Poor-risk patients (inadequate bone marrow reserve, abnormal liver function) receive a reduced dose, 1.6 mg/sqm HAI, on the same schedule. All patients who achieve at least a partial response after 2 cycles of Chemotherapy continue treatment until complete remission or progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/80

1.0065 PHASE II CHEMOTHERAPY WITH PROCARBAZINE FOR BREAST CANCER

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PROTOCOL NUMBER(S) MDAR-421; MDA-MBDT-8047

OBJECTIVES:

I. Determine the efficacy of procarbazine administered by oral intermittent schedule to patients with breast cancer.

II. Determine the qualitative and quantitative toxicity of procarbazine administered in this fashion.

III. Determine the duration of response and duration of survival of patients receiving this therapy.

IV. Serve as a pilot study for a later Phase I/II study of the efficacy of procarbazine administered by intermittent intravenous schedule to patients with breast cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic breast cancer with clearly measurable lesions who are not candidates for known regimens or protocol treatments of higher priority. Patients must have a life expectancy of at least 12 weeks, and there must be adequate bone marrow function. Patients must have been off all previous chemotherapy, radiotherapy, or immunotherapy for the 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Procarbazine, PCB, NSC-77213.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests, tumor measurements.

END POINTS: Response/remission rate, disease-free interval, duration of response, objective tumor response, survival.

CURRENT STATUS: 25-30 patients will be entered, unless all first 14 patients fail to respond.

DOSAGE SCHEDULE:

PCB - 200 mg/sqm po for 21 days q 28 days. Poor-risk patients (inadequate bone marrow, liver, or renal function) receive a reduced dose, 150 mg/sqm po, on the same schedule. Chemotherapy is continued for 2 years or for 1 year after patient achieves complete remission, whichever is shorter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

1.0066 CHEMOTHERAPY WITH 5-FU/ADR/CTX, IMMUNOTHERAPY WITH BCG, AND MASTECTOMY AND RADIOTHERAPY FOR CATEGORY IV BREAST CARCINOMA

Montague, E., (713-792-3400) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-43

OBJECTIVES: None given.

PROTOCOL ENTRY CRITERIA: Enter patients with edema, ulceration and skin fixtures over more than one-half of the breast with peripheral satellite nodules. Tumor can be fixed to chest wall. Axillary nodes are fixed and large, and supraclavicular nodes are present.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Immunotherapy plus Surgery plus Radiotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; plus BCG, unspecified; Cobalt-60 Radiotherapy; plus Surgery (a simple or extended simple mastectomy).

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: None given.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

5-FU; ADR; CTX, given following biopsy - no dosage details given. Radiotherapy for patients with good regression: Cobalt-60 to all areas - 5000 rads to breast, axilla, supraclavicular and internal mammary areas with boost of 1000-1500 rads in 5 to 7 days to quadrant of primary and any peripheral nodes palpable prior to Chemotherapy. Surgery for patients with poor regression and non-inflammatory tumors: simple or extended simple mastectomy followed by Radiotherapy: Cobalt-60 - 5000 rads to entire scar and chest wall, axilla, supraclavicular and internal mammary node lymphatics over 5 weeks, plus 1000 rads over 4 to 5 days to areas of increased risk. Additional 5-FU, ADR, CTX, and BCG are given for 2 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/77

1.0067 ADJUVANT CHEMOTHERAPY WITH CMF (CTX/MTX/5-FU) OR LMF (CLB/MTX/5-FU) WITH OR WITHOUT LEVAMISOLE FOR HIGH-RISK BREAST CANCER

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PROTOCOL NUMBER(S) MSKCC-7454

OBJECTIVES:

I. Reduce the rate of recurrence and lengthen the disease-free interval after surgery.

II. Measure immune reactivity in patients with breast cancer treated with chemotherapy or immunotherapy.

PROTOCOL ENTRY CRITERIA: Patients with primary operable infiltrating breast cancer including those with any macroscopic axillary node metastases or micrometastases at level III, and patients with negative axillary nodes whose infiltrating tumors are greater than 2 cm in diameter.

PROTOCOL OUTLINE: Randomized study. Following modified, standard or extended radical mastectomy, randomize patients with positive nodes to Arms I or II; those with negative nodes to Arm III or IV.

Arm I: 3-Drug Combination Chemotherapy. CMF: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 3-Drug Combination Chemotherapy plus Immunotherapy. CMF; plus Levamisole, LEV, NSC-177023.

Arm III: 3-Drug Combination Chemotherapy. LMF: Chlorambucil, CLB, NSC-3088; MTX; 5-FU.

Arm IV: 3-Drug Combination Chemotherapy plus Immunotherapy. LMF; plus LEV.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CMF: CTX - 100 mg/sqm/day po on days 1 through 14; MTX -40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8. Repeat course following a 2-week rest period.

Arm II: CMF: as in Arm I; plus LEV - 150 mg on days 8, 9, 10, 22, 23 and 24 of each course.

Arm III: CLB - 6 mg/day po on days 1 through 14; MTX - 25 mg po on days 1 and 8; 5-FU - 500 mg po on days 1 and 8. Repeat course q 28 days for 2 years.

Arm IV: LMF - as in Arm I; plus LEV - as in Arm II.

Dosage modifications for patients over 65 years of age are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/78

1.0068 CHEMOTHERAPY WITH VINBLASTINE/ADRIAMYCIN/THIOTEPA PLUS FLUOXYMESTERONE FOR METASTATIC OR SURGICALLY INCURABLE BREAST CARCINOMA

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PROTOCOL NUMBER(S) MTS-18

OBJECTIVES:

I. Develop an effective, convenient, second line treatment with VATH: vinblastine/adriamycin/thiotepa/fluoxymesterone for patients with metastatic breast cancer.

II. Assess the efficacy of VATH chemotherapy when all intravenous chemotherapy is given on Day 1 of each cycle. Treatment cycles will be repeated at 3 weekly intervals if toxicity from the previous cycle has resolved.

III. Improve the response rate and duration of remission by increasing the dose of adriamycin over the last study.

IV. Establish a treatment procedure on a pilot basis that is suitable for broad scale definitive study in a cooperative group.

PROTOCOL ENTRY CRITERIA: Patients less than 70 years of age with histologically-proven metastatic or surgically incurable mammary carcinoma, who have had prior chemotherapy with cyclophosphamide, methotrexate, and 5-fluorouracil with or without vincristine and prednisone for Stages II, III, or IV breast cancer. Patients must have adequate hematologic and cardiac function and normal renal and hepatic function (unless abnormalities are due to metastatic involvement).

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. VATH: Adriamycin, ADR, NSC-123127; Vinblastine, VBL, NSC-49842; Thiotepa, NSC-6396; plus Fluoxymesterone, FXM, NSC-12165.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: SMA-18, bone survey, liver and bone scan.

END POINTS: Objective tumor response, response/remission rate, time to progression, toxicity/morbidity of treatment, duration of remission.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

VATH: ADR - 45 mg/sqm (total maximum dose 550 mg/sqm); VBL - 4.5 mg/sqm; Thiotepa - 12 mg/sqm; all given iv in series in separate syringes on day 1 q 21 days, providing recovery from toxicity of previous cycle has taken place; Fluoxymesterone - 30 mg/day po in 3 divided doses. Keep patients who demonstrate response, improvement, or no change after 2 cycles of treatment on study until disease progression or development of unacceptable toxicity. Remove patients with disease progression after 2 cycles from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/78

1.0069 ORCHIECTOMY WITH OR WITHOUT SUBSEQUENT ADRENALECTOMY FOR METASTATIC CANCER OF THE MALE BREAST

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PROTOCOL NUMBER(S) NCI-76-C-198; NCI-MB-52

OBJECTIVES:

I. Evaluate the hormone dependence of male breast cancer and the effectiveness of endocrine manipulations in relation to serum, urine, and tumor concentrations of testosterone, cortisol, ACTH, FSH, LH, prolactin, and estrogen.

II. Correlate hormone receptor activity in the tumor with the response to therapeutic hormonal procedures.

III. Evaluate the therapeutic efficacy of adrenalectomy following relapse or failure after orchiectomy in these patients.

PROTOCOL ENTRY CRITERIA: Males with metastatic breast cancer who have not received prior hormonal therapy. Patients may have relapsed while on adjuvant chemotherapy. Patients should have tumors that can be biopsied for hormone receptor activity, but those without biopsiable tumors will be accepted and evaluated separately. Bone marrow, liver, and kidney function must be adequate. The Karnofsky performance status must be greater than 40, and patients may not have had earlier cancers other than cured squamous or basal cell carcinoma of the skin.

PROTOCOL OUTLINE: Nonrandomized study. All patients enter Regimen A. Subsequently, those able to tolerate adrenalectomy enter Regimen B and others enter Regimen C.

Regimen A: Surgery. Orchiectomy.

Regimen B: Adrenalectomy plus Replacement Hormone Therapy. Dexamethasone, DM, NSC-34521; Florinef, NSC-15186.

Regimen C: Medical Adrenalectomy plus Replacement Hormone Therapy. Aminoglutethimide, no NSC number; DM; Florinef.

STRATIFICATION BY: Prior adjuvant chemotherapy (yes vs. no), availability of tumor for biopsy (yes vs. no).

SPECIAL STUDY PARAMETERS: Bone and liver scan, chest x-ray, gallium scan, hormone receptor assays (tumor tissue, serum, urine), ACTH stimulation test, hemogram, liver and kidney function tests, appropriate tumor measurements.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Following orchiectomy, patients are observed for up to 12 weeks. Patients proceed to Regimen B (Regimen C for patients unable to tolerate surgery) upon the development of progressive disease. Those who respond to orchiectomy and subsequently relapse proceed to Regimen B. Patients whose disease is stabilized following castration will be observed if there is a subjective response and if the performance index is at least 70 and the analgesia index is not greater than 2; otherwise they will undergo adrenalectomy.

Regimen B: Adrenalectomy. DM - 1.5 mg/day; Florinef - 0.1 mg/day.

Regimen C: Aminoglutethimide - 1.0 g/day; DM - 1.5-3 mg/day; Florinef - 0.1 mg/day.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

1.0070 CHEMOTHERAPY WITH CTX/ADR/5-FU/MTX WITH AND WITHOUT CELL SYNCHRONIZATION WITH TAMOXIFEN AND PREMARIN FOR METASTATIC BREAST CARCINOMA

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PROTOCOL NUMBER(S) NCI-76-C-377

OBJECTIVES:

I. Measure response rates, duration of responses, and proportion of CR in patients with metastatic breast carcinoma treated with cyclophosphamide/adriamycin/5-fluorouracil/methotrexate with and without tamoxifen and Premarin.

II. Assess the ability of hormonal therapy to synchronize tumor cells by conducting kinetic studies in a small proportion of patients with readily biopsied disease.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented breast carcinoma who have measurable and progressive disease. Patients may not have received previous cytotoxic therapy except adjuvant L-phenylalanine mustard. Patients must be under 65 years of age and have a Karnofsky performance status greater than 30. There must be evidence of adequate bone marrow, renal, and hepatic function, and there must be no history of malignant neoplasms (except curatively treated basal cell or squamous cell carcinoma of the skin or surgically cured carcinoma of the cervix in situ).

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy. CTX; ADR; 5-FU; MTX; plus Tamoxifen, TMX, NSC-180973; Premarin (conjugated estrogens).

STRATIFICATION BY: Estrogen receptor status (positive vs. negative vs. unknown); previous hormonal therapy (yes vs. no); menopausal status; dominant disease site (brain, hepatic, lymphangitic, pulmonary vs. other); Karnofsky index (60 or greater vs. less than 60); previous L-phenylalanine mustard (yes vs. no).

SPECIAL STUDY PARAMETERS: Hemogram, blood groupings, HL-A, immunoglobullins, liver and kidney function tests, chest x-rays, tomograms of lesions, liver and bone scan, brain and gallium scan, vaginal cytology, bone marrow aspiration and biopsy, ophthalmologic examinations, kinetic studies, EKG, metastatic survey.

END POINTS: Response/remission rates, duration of response, objective tumor measurement, toxicity/morbidity of treatment.

CURRENT STATUS: 80 patients will be entered over a period of about 1.5 years, with an additional 2 years required for followup.

DOSAGE SCHEDULE:

Arm I: CTX - 750 mg/sqm iv on day 1; ADR - 30 mg/sqm iv on day 1, to be discontinued after a total cumulative dose of 550 mg/sqm; 5-FU - 500 mg/sqm iv on day 8; MTX - 40 mg/sqm iv on day 9. Repeat q 21 days.

Arm II: CTX, ADR, 5-FU, and MTX as in Arm I; plus TMX - 20 mg/sqm po in 2 equally divided doses on days 2 through 6; Premarin - 0.625 mg po q 12 hours for a total of 3 doses beginning on the morning of day 7. Repeat q 21 days.

Patients with progressive disease after 2 cycles will go off study. After achieving CR, patients will be given 17 cycles of Chemotherapy, alternating cycles including ADR.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 20 mg vials; CTX - 100, 200, and 500 mg vials; 5-FU - 500 mg ampules; MTX - 5 and 50 mg vials.

DATE SUMMARIZED: 10/80

1.0071 MASTECTOMY AND AXILLARY DISSECTION VS EXCISIONAL BIOPSY, AXILLARY DISSECTION AND DEFINITIVE RADIOTHERAPY FOR STAGE I-II BREAST CARCINOMA

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PROTOCOL NUMBER(S) NCI-79-C-111

OBJECTIVES:

I. Compare mastectomy and axillary dissection with definitive radiotherapy and axillary dissection, using ancillary chemotherapy for subjects with positive nodes in both groups, in patients with Stage I-II breast carcinoma.

II. Study relapse location, complications of therapy, anatomic function, and cosmesis in these 2 groups of treated patients.

PROTOCOL ENTRY CRITERIA: Women with biopsy-proven, untreated breast carcinoma of clinical Stages I and II. The tumor must not be inflammatory, and there may be no other concurrent chronic disease. Disease may not be bilateral, nor may there be multiple masses or multiple suspicious areas on mammogram. Patients assigned to chemotherapy must have adequate bone marrow, liver, and kidney function and no history of ischemic heart disease, cardiomyopathy, or congestive heart failure.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I and II. Postoperatively, enter those patients from Arms I and II with negative axillary nodes to Regimen A and those patients with positive nodes to Regimen B.

Arm I: Primary Surgery.

Arm II: Radiotherapy plus Surgery. External Radiotherapy - 4 and 6 MeV linear accelerator; Implantation Radiotherapy - Iridium or Cesium seeds in an interstitial implant.

Regimen A: No further treatment.

Regimen B: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: Age (younger than 50 vs. 50 or older), nodal status (clinically active vs. clinically negative, and histologically positive vs. histologically negative).

SPECIAL STUDY PARAMETERS: Hemogram, SMA-21, EKG, chest x-ray and bone survey, brain and liver scans, bone scan, breast photography, lymphoscintigram of internal mammary nodes, CT chest scan, chest ultrasound.

END POINTS: Absolute survival time from time of diagnosis, determinant survival from time of diagnosis, relapse rate, relapse locations, complications of therapy, anatomic function, cosmesis.

CURRENT STATUS: About 250 patients will be entered over 5 years.

DOSAGE SCHEDULE:

Arm I: Total Mastectomy with Axillary Dissection. Subsequently, patients with negative axillary nodes enter Regimen A and those with positive nodes enter Regimen B.

Arm II: Excisional Biopsy and Axillary Dissection. Radiotherapy: 4500-5000 rads to the breast, chest wall, and internal mammary nodes over 5-5.5 weeks. The supraclavicular field, when treated, will receive 4500-5000 rads over 5-5.5 weeks; if the axilla contains gross residual tumor after surgery, dose to the axilla will be boosted to 6000-6500 rads over 6-7.5 weeks. Implantation therapy - 2000-3000 rads over 1.5-3 days, using Iridium or Cesium seeds, to the tumor bed. Patients proceed to Regimen A or Regimen B on the basis of nodal status, as in Arm I. Regardless of subsequent treatment, patients undergo total mastectomy upon the development of recurrent disease in the breast.

Regimen A: Observe.

Regimen B: ADR - 30 mg/sqm iv on day 1; CTX - 150 mg/sqm/day po on days 3 through 6. Begin treatment as soon after surgery as possible. Start second cycle on day 49, and repeat at 28-day intervals. In the absence of significant myelosuppression, escalate CTX to 175 mg/sqm after 3 cycles and to 200 mg/sqm after 5 cycles. Discontinue adjuvant therapy when the total cumulative ADR dose reaches 330 mg/sqm.

Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/80

1.0072 CHEMOTHERAPY WITH CTX/MTX/5-FU AND/OR IMMUNOTHERAPY WITH BCG IN DISSEMINATED BREAST CANCER

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PROTOCOL NUMBER(S) MI-BR-1

OBJECTIVES:

I. Compare the survival rate for disseminated breast cancer patients receiving BCG immunotherapy and 3-drug combination chemotherapy (cyclophosphamide/methotrexate/5-fluorouracil), alone and in combination, with survival rate of those receiving no therapy.

PROTOCOL ENTRY CRITERIA: Patients with Stage IV disseminated breast cancer who have undergone surgery for the removal of the primary tumor.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. CMF: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm III: 3-Drug Combination Chemotherapy plus Immunotherapy. CMF; BCG.

Arm IV: No further therapy.

STRATIFICATION BY: Participating institutions; staging by the American Joint Committee.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 50 patients will be entered.

DOSAGE SCHEDULE:

Arm I: CMF: CTX - 100 mg/sqm po on days 1-14; MTX - 60 mg/sqm, in patients less than 60 years (30 mg/sqm in those over 60 years), iv on days 1 and 8; 5-FU - 600 mg/sqm, in patients less than 60 years (400 mg/sqm in those over 60 years), iv on days 1 and 8. CMF will be administered in a 2-week course followed by a 2-week rest period for 4 cycles, then a 3-week course followed by a 4-week rest period, covering a period of 106 weeks.

Arm II: BCG - no dosage specified. Treatment will be started during week 3, given every week for 11 weeks (through week 13), then every other week through week 106. BCG is administered by the tine technique percutaneous in both axillae or deltoid areas and both groin areas.

Arm III: CMF - as in Arm I; BCG - as in Arm II, after 2 weeks of CMF.

Arm IV: No further therapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 2-8 x 10 to the eighth colony-forming units per ampule.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

1.0073 BCG IMMUNOTHERAPY, CMF CHEMOTHERAPY, AND RADIOTHERAPY, ALONE AND IN VARIOUS COMBINATIONS FOR BREAST CANCER

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PROTOCOL NUMBER(S) MI-BR-2

OBJECTIVES:

I. Compare the cure rates of patients with potentially curative breast cancer and histologically proven metastases to the axillary nodes using: (1) immunotherapy with BCG alone, (2) chemotherapy with CMF (CTX/MTX/5-FU) alone, (3) radiation therapy alone; (4) BCG and CMF in combination; and (5) BCG, CMF and radiation therapy in combination.

PROTOCOL ENTRY CRITERIA: All patients who have had a conventional or modified radical mastectomy for potentially (clinically) curable breast cancer with histologically proven metastases to the axillary nodes.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. CMF: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Immunotherapy. BCG-Tice, BCG, NSC-116327.

Arm III: Radiotherapy.

Arm IV: 3-Drug Combination Chemotherapy plus Immunotherapy. CMF; BCG.

Arm V: 3-Drug Combination Chemotherapy plus Immunotherapy plus Radiotherapy. CMF; BCG; Radiotherapy.

STRATIFICATION BY: Participating institutions; staging by the American Joint Committee.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 10-20 patients.

DOSAGE SCHEDULE:

Arm I: CMF: CTX - 100 mg/sqm po days 1-14; MTX - 60 mg/sqm in patients younger than 60 (30 mg/sqm in those older than 60) iv days 1, 8; 5-FU - 600 mg/sqm (400 mg/sqm in those older than 60) iv days 1, 8. CMF will be administered in a two-week course followed by a two-week period off treatment in four cycles and then a two-week course followed by a four-week period off treatment, covering a total period of 106 weeks.

Arm II: BCG - no dosage specified. Treatment begins on week 3 (after 2 weeks of CMF), every week for 11 weeks (through week 13), then every other week to 106 weeks, by the tine technique percutaneous in both axillae or deltoid areas and both groin areas.

Arm III: Radiotherapy. (No details given.)

Arm IV: CMF and BCG - as in Arms I and II.

Arm V: CMF, BCG, and Radiotherapy - as in Arms I, II and III.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 2-9 x 10 to the eighth colony-forming units per ampule.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

1.0074 CHEMOTHERAPY WITH ADR/CTX WITH OR WITHOUT RADIOTHERAPY OR CHEMOTHERAPY WITH L-PAM FOR THE ELIMINATION OF MICROMETASTASES IN BREAST CANCER

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PROTOCOL NUMBER(S) UARIZ-674; UARIZ-IVB

OBJECTIVES:

I. Assess the effectiveness of combination chemotherapy with cyclophosphamide (CTX)/adriamycin (ADR) in eliminating micrometastases after completion of initial treatment in patients with the greatest risk of both distant metastases and local recurrence of breast cancer.

II. Assess the ultimate effect of extensive adjuvant chemotherapy on the disease-free survival and overall survival of patients with carcinoma of the breast.

III. Determine the frequency of abnormal bone scans in patients with cancer of the breast that would otherwise be classified as Stage II.

IV. Assess the influence of abnormal and equivocally abnormal bone scans on the ultimate natural history of breast cancer after completion of initial treatment.

PROTOCOL ENTRY CRITERIA: Patients under 65 with proven pathological Stage II infiltrating ductal or lobular (Amendment 1) carcinoma. Patients must have undergone radical or modified radical mastectomy and be at risk of local and distant recurrence.

PROTOCOL OUTLINE: Randomized study. Enter all patients at highest risk for recurrence to Arm I. (Amendment 3). For patients at intermediate risk, randomize 2 patients to therapy in Arm I or Arm II for each patient randomized to Arm III. Enter patients who decline Arm I or II Chemotherapy to Regimen A. Stage I breast cancer patients may be entered to Arm II, 3 courses only (Amendment 2).

Arm I: 2-Drug Combination Chemotherapy, plus Radiotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; plus 4 MeV x-ray therapy.

Arm II: 2-Drug Combination Chemotherapy. CTX, ADR.

Arm III: No further therapy.

Regimen A: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

STRATIFICATION BY: Prior radiotherapy, results of bone scan, menopausal status, number of positive axillary nodes.

SPECIAL STUDY PARAMETERS: Bone scan, cardiac studies, liver function tests.

END POINTS: Time to recurrence, recurrence rate, survival time, survival rate.

CURRENT STATUS: 150 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Begin within 1 month following surgery; ADR - 30 mg/sqm iv on day 1 q 3 weeks, CTX 150 mg/sqm po on days 3 through 6 q 3 weeks. Give 2 courses, the first at 75% of full dosage. Enter patients to Radiotherapy - 4400 rads given in 4.5 weeks to the chest wall and supraclavicular and internal mammary nodes. Then give an additional 6 courses of Chemotherapy.

Arm II: ADR, CTX as in Arm I, 8 consecutive courses.

Arm III: No therapy.

Regimen A: L-PAM - 0.75 mg/kg (route not given) q 6 weeks for 2 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/78

1.0075 PHASE III COMBINATION CHEMOTHERAPY WITH VAC (VCR/ADR/CTX) VS CMF (CTX/MTX/5-FU) FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) WFU-POA-74379

OBJECTIVES:

I. Determine the response rate, duration of response and toxicity for two combination chemotherapy programs, VAC: vincristine (VCR)/adriamycin (ADR)/cyclophosphamide (CTX) and CMF: CTX/methotrexate (MTX)/5-fluorouracil (5-FU) in patients with advanced breast cancer.

II. Determine the relationship of estrogen and progesterone activity to response rate and duration.

PROTOCOL ENTRY CRITERIA: Patients with measurable or evaluable, histologically proven metastatic breast cancer. Patients must be between 18 and 75 years of age, with adequate cardiac and hematologic status. Patients must have no prior therapy with the study agents.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. VAC: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm II: 3-Drug Combination Chemotherapy. CMF: CTX; Methotrexate, MTX, NSC-740; 5-Fluorouracil; 5-FU, NSC-19893.

STRATIFICATION BY: Estrogen receptor status: positive vs. equivocal vs. negative vs. unknown.

SPECIAL STUDY PARAMETERS: SMAC; bone, liver and brain scans.

END POINTS: Objective tumor response, duration of response, survival duration.

CURRENT STATUS: 240 patients to be entered in 1 to 2 years.

DOSAGE SCHEDULE:

Arm I: VAC: VCR - 1 mg/sqm (maximum dose 2 mg) iv on day 1; ADR - 40 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on day 1; CTX - 200 mg/sqm po on days 3 through 6. Repeat q 3 weeks for 1 year then q 4 weeks. Omit ADR when maximum dose is reached.

Arm II: CMF: CTX - 350 mg/sqm iv on day 1; MTX - 20 mg/sqm iv on day 1; 5-FU - 350 mg/sqm iv on day 1. Repeat q 3 weeks for 1 year then q 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

1.0076 PHASE II CHEMOTHERAPY WITH VAC (VCR/ADR/CTX) PLUS ENDOCRINE THERAPY WITH MPA FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) AIO-GO-MC-I/80

OBJECTIVES:

I. Determine the therapeutic index of VAC (vincristine/adriamycin/cyclophosphamide) plus medroxyprogesterone acetate (MPA) in patients with metastatic breast cancer.

PROTOCOL ENTRY CRITERIA: Patients with measurable, metastatic breast cancer. Karnofsky performance status must be at least 60, and there may be no evidence of heart disease.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. VAC: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; plus Medroxyprogesterone acetate, MPA, NSC-26386.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Hematologic, liver, and kidney function tests; CEA; immunocomplexes; hormone profiles; blood levels of MPA.

END POINTS: Response/remission rate, duration of remission.

CURRENT STATUS: 120 patients will be entered.

DOSAGE SCHEDULE:

VAC: VCR - 1 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 1; CTX - 200 mg/sqm po on days 3 through 6; repeat every 21 days. MPA - 1500 mg po daily for 6 weeks, then (upon remission) 500 mg po daily. Patients showing progression after 2 cycles are removed from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 01/81

1.0077 PHASE II ENDOCRINE THERAPY WITH MPA/AGT FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) AIO-GO-MC-II/80

OBJECTIVES:

I. Determine the therapeutic activity and toxicity of the combination of medroxyprogesterone acetate (MPA) and aminoglutethimide (AGT) in patients with metastatic breast cancer.

II. Determine whether MPA compensates for adrenal insufficiency induced by AGT.

III. Correlate results of therapy with biological variables, risk and prognostic factors, immune complexes, hormone profiles, lipid status, and MPA blood levels.

PROTOCOL ENTRY CRITERIA: Patients with metastatic breast cancer previously treated by ovariectomy or tamoxifen (in estrogen-receptor-positive patients) or by first choice chemotherapy (in estrogen-receptor-negative patients). Minimum life expectancy must be at least 2 months, and Karnofsky performance status 60 or better.

PROTOCOL OUTLINE: Nonrandomized study. Patients elect treatment on Regimen A or Regimen B.

Regimen A: 2-Drug Endocrine Therapy. Aminoglutethimide, AGT, no NSC number; Medroxyprogesterone acetate, MPA, NSC-26386, administered orally.

Regimen B: 2-Drug Endocrine Therapy. AGT; MPA, administered intramuscularly.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Hematologic, liver, and kidney function tests; blood levels of MPA; hormone profiles; cell cultures.

END POINTS: Response/remission rate, duration of remission.

CURRENT STATUS: 60 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: AGT - 1 g/day po for 6 weeks; MPA - 1500 mg/day po in 3 divided doses for 6 weeks, then 500 mg/day po upon remission. Patients showing progression after 6 weeks go off study.

Regimen B: AGT - 1 g/day po; MPA - 500 mg/day im for a minimum of 6 weeks, and, upon remission, 1 g/week im. Patients showing progression after 6 weeks go off study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: AGT - 250 mg tablets; MPA - 100 and 200 mg tablets and 500 mg vials.

Summary as provided by investigator.

DATE SUMMARIZED: 01/81

1.0078 PHASE III HORMONE THERAPY WITH MPA FOR METASTATIC BREAST CANCER REFRACTORY TO CHEMOTHERAPY

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PROTOCOL NUMBER(S) AIO-GO-MC-III/80

OBJECTIVES:

I. Determine the therapeutic efficacy of high-dose medroxyprogesterone acetate (MPA) in patients with metastatic breast cancer resistant to adriamycin, cyclophosphamide, 5-fluorouracil, methotrexate, and vincristine.

II. Assess the practicability of administering MPA intramuscularly vs. orally.

PROTOCOL ENTRY CRITERIA: Patients with metastatic breast cancer resistant to adriamycin, cyclophosphamide, 5-fluorouracil, methotrexate, and vincristine. The Karnofsky performance status must be at least 60.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Hormone Therapy. Medroxyprogesterone acetate, MPA, NSC-26386. Oral administration.

Arm II: Single-agent Hormone Therapy. MPA. Intramuscular administration.

STRATIFICATION BY: Menopausal status, disease-free interval, site of metastases, body weight, estrogen receptor status, Karnofsky status, prior chemotherapy (beneficial or not).

SPECIAL STUDY PARAMETERS: Hormone profiles, immune complexes, lipid status, blood levels of MPA.

END POINTS: Response/remission rate, duration of remission, toxicity of treatment.

CURRENT STATUS: 90 patients will be entered.

DOSAGE SCHEDULE:

Arm I: MPA - 1500 mg/day po on days 1 through 42, reduced upon achievement of remission or stable disease to 500 mg/day po.

Arm II: MPA - 500 mg/day im on days 1 through 42, reduced upon achievement of remission or stable disease to 1000 mg/week im.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 01/81

1.0079 COMBINATION CHEMOTHERAPY WITH CTX/MTX OR CTX/5-FU FOR ADVANCED CARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) ARG-BR-118

OBJECTIVES:

I. Avoid the use of oral cyclophosphamide (CTX) and the possible antagonism between 5-fluorouracil (5-FU) and methotrexate (MTX).

II. Determine whether alternating therapies with CTX/MTX and CTX/5-FU increases the disease-free period (complete remission) and length of survival in patients with advanced carcinoma of the breast.

PROTOCOL ENTRY CRITERIA: Patients with histologic evidence of Stage IV breast cancer. Patients may have had prior suppressive or additive hormone therapy. Prior hormone therapy must have been withdrawn at least 3 months prior to entry. Performance status of at least 50% is required, and there must be no concurrent or previous malignancy in other sites (except for cervical carcinoma in situ or adequately treated basal or squamous cell carcinoma of the skin).

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Radioisotopic scans of brain, bone and liver; CAT; mammography; bone marrow biopsy; laparoscopy; ultrasonography; immunologic evaluation; photographic or radiologic measurement of lesions.

END POINTS: Disease-free interval, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 50-100 patients will be entered.

DOSAGE SCHEDULE:

CTX - 600 mg/sqm on days 1 and 8; MTX - 50 mg/sqm on day 1; 5-FU - 600 mg/sqm on day 8. Repeat q 28 days. CR patients complete 6 additional courses for Consolidation. PR patients continue treatment until CR or progression. Patients with stable disease continue treatment until progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

1.0080 PHASE I-II CHEMOTHERAPY WITH FTORAFUR FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) ARG-HR-3005

OBJECTIVES:

I. Verify the response to Ftorafur of patients with advanced breast cancer.

II. Determine the maximum tolerated dose of Ftorafur, the minimum time interval between two courses and the time after which treatment can be repeated.

III. Determine the toxicity of Ftorafur.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with advanced inoperable and/or metastatic and/or recurrent histologically confirmed breast carcinoma. Patients must have at least one evaluable lesion, a minimum life expectancy of 3 months, a Karnofsky performance status better than 30%, and they must have adequate liver, bone marrow and renal function. Patients must be ambulatory and must not have had any therapy for their disease for 2 months and no P-32 for 1 year prior to study entry.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I, II, and III: Single-agent Chemotherapies. Ftorafur, NSC-148958; different doses.

Regimen A: For nonresponders to Ftorafur. 3-Drug Combination Chemotherapy. 5-FU, NSC-19893; Cyclophosphamide, CTX, NSC-26271; Vinblastine, VBL, NSC-49842.

STRATIFICATION: Premenopausal: more vs. less than 1 year from oophorectomy vs. post-menopausal: disease-free interval; concurrent vs. 1 to 5 years vs. more than 5 years; site of dominant lesion: visceral: pulmonary vs. hepatic vs. cerebral, vs. osseous vs. soft tissue.

SPECIAL STUDY PARAMETERS: Scintiscans of liver, cerebrum, bones; skin tests for recall antigens; in vitro lymphocyte reactions; immunoglobulin levels; serum complement: C3 fraction; enzyme studies.

END POINTS: Response/remission rate, duration of remission, survival time, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: About 30 patients will be entered in one year.

DOSAGE SCHEDULE:

Induction:

Give all therapy for 5 days q 3 weeks.

Arm I: Ftorafur - 400 mg/sqm po.

Arm II: Ftorafur - 600 mg/sqm po.

Arm III: Ftorafur - 800 mg/sqm po.

Give 8 courses of Ftorafur to patients with objective regression of disease. Give 3 courses to patients with no change in disease status, then enter to regimen A. Enter nonresponders and patients with progressive disease to regimen A.

Regimen A: FU - 600 mg/sqm iv on days 1 through 5; CTX - 400 mg/sqm iv on day 1; VBL - 6 mg/sqm iv on day 1. Repeat course q 3 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS:

Ftorafur - 200 mg capsules.

DATE SUMMARIZED: 10/79

1.0081 PHASE III COMBINATION CHEMOTHERAPY WITH CTX/VBL/5-FU WITH OR WITHOUT TAMOXIFEN FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) ARG-OSITC-4003

OBJECTIVES:

I. Determine whether the addition of tamoxifen to the combination of cyclophosphamide (CTX), vinblastine (VBL), and 5-fluorouracil (5-FU) can improve the frequency and duration of remissions.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed advanced breast cancer, in situ, metastatic or relapsed, who have at least one objectively evaluable lesion. A minimum life expectancy of 3 months and a Karnofsky performance status greater than 30 percent are required. Prior radiation therapy or chemotherapy must have been performed at least 2 months prior to entry, and patients may not have received P-32 during the preceding year. An elapse of 4 weeks must obtain following prior hormonal therapy (more than 8 weeks for osteolytic metastases). Surgical hormonal suppressive therapy must have ended 8 weeks prior to entry (12 weeks for osteolytic lesions). Blood counts, hepatic function, and blood chemistry must meet stated requirements. Long-range followup must be possible.

PROTOCOL OUTLINE: Randomized study. Nonresponders to Arm I or Arm II treatment enter Regimen A.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. 5-Fluorouracil, 5-FU, NSC-19893; Cyclophosphamide, CTX, NSC-26271; Vinblastine, VBL, NSC-49842; plus Tamoxifen, TMX, NSC-180973.

Arm II: 3-Drug Combination Chemotherapy. 5-FU; CTX; VBL.

Regimen A: 3-Drug Combination Chemotherapy. 5-FU; CTX; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Hormonal status: premenopausal vs. postmenopausal; disease-free interval: less than 1 year vs. 1 to 5 years vs. more than 5 years; site of primary lesion: visceral vs. bone vs. soft tissue.

SPECIAL STUDY PARAMETERS: Skeletal radiography; hepatic, cerebral, and bone scintigrams; CAT; EEG.

END POINTS: Response/remission rate, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 100 evaluable patients will be entered.

DOSAGE SCHEDULE:

Arm I: 5-FU - 600 mg/sqm iv perfusion on days 1 to 5; CTX - 400 mg/sqm iv on day 1; VBL - 4 mg/sqm iv on day 1. Repeat cycle after day 21. TMX - 20 mg/day po in 2 divided doses for duration of treatment. Patients showing objective regression complete 8 courses; those with stable disease or progressive disease after 3 courses enter Regimen A.

Arm II: 5-FU; CTX; VBL given as in Arm I. Responders complete 8 courses of treatment. Those with stable or progressive disease after 3 courses enter Regimen A.

Regimen A: 5-FU - 600 mg/sqm iv perfusion on days 1 and 8; ADR - 40 mg/sqm iv on day 1; CTX - 60 mg/sqm po on days 1 to 10. Repeat cycle after day 21.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - 10 mg tablets; other drug forms are not given.

DATE SUMMARIZED: 08/80

1.0082 CHEMOTHERAPY WITH FAC (5-FU/ADR/CTX) PLUS IMMUNOTHERAPY WITH LEV VS BCG FOR STAGE IV BREAST CARCINOMA

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PROTOCOL NUMBER(S) ARG-RNH-2981

OBJECTIVES:

I. Determine the best combination for the remission induction frequency and duration by comparing 3-drug combination chemotherapy FAC: 5-fluorouracil (5-FU)/adriamycin (ADR)/cyclophosphamide (CTX) plus immunotherapy using levamisole (LEV) vs. BCG for Stage IV breast carcinoma.

II. Test whether the addition of levamisole or BCG increases the remission induction frequency or prolongs the remission duration or both, and to determine whether levamisole or BCG alters the tolerance of normal tissues to these combined chemotherapeutic programs.

III. Establish the initial immunocompetence of patients with metastatic breast cancer as determined by skin recall antigens (PPD, Mumps, SK/SD), DNCB skin test, lymphocyte blastogenesis, etc.; assess whether the administration of levamisole or BCG alters that initial status; and determine if any changes are associated with prolonged disease control.

IV. Evaluate the beneficial effects of levamisole immunotherapy and of BCG immunotherapy.

V. Compare the remission induction frequency and duration of the FAC with levamisole or BCG with that of FAC alone.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed breast carcinoma, and with no prior chemo- or immunotherapy. Patient must have minimum life expectancy of 3 months and performance status of 50 percent or more (by Karnofsky table). No signs of systemic infection or other neoplastic disease must be present. Adequate hepatic and renal functions must obtain. Peripheral blood counts must be above 3,500,000 RBC, 3800 WBC and 150,000 thrombocytes per cubic millimeter.

PROTOCOL OUTLINE: Randomized study.

Induction: 6 cycles.

Arm I: 3-Drug Combination Chemotherapy plus Immunotherapy. FAC: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271, plus Levamisole, LEV, NSC-177023.

Arm II: Chemotherapy as in Arm I. Immunotherapy, BCG-Pasteur, BCG, NSC-B116328.

Maintenance:

Arm I and Arm II: 3-Drug Combination Chemotherapy: 5-FU; Vincristine, VCR, NSC-67514; Methotrexate, MTX, NSC-740. Adjuvant Immunotherapy: Arm I, LEV; Arm II, BCG.

STRATIFICATION BY: Age: 0-20 years, 20-40, 40-60, more than 60; location of metastases; post-menopausal status: more or less than 5 years; prior therapy; immune status.

SPECIAL STUDY PARAMETERS: Ficoll-Hypaque Test, Candidina, ECG, Scintigram, Echocardiogram.

END POINTS: Toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: Repeat course every 3 weeks for 6 cycles.

Arm I: 5-FU - 500 mg/sqm iv days 1 and 8; ADR - 50 mg/sqm iv day 1; CTX - 500 mg/sqm iv day 1. Levamisole - 150 mg/day po for 3 consecutive days, followed by free period of 15 days.

Arm II: Chemotherapy as in Arm I plus Immunotherapy with BCG - 6 x 10 to the eighth vial units by scarification on days 9, 13, and 17.

Maintenance: Repeat course every 4 weeks for 10 cycles.

Arm I: 5-FU - 500 mg/sqm iv days 1 and 8; VCR - 1.4 mg/sqm iv day 1 (6 hours before 5-FU); MTX - 15 mg/sqm iv days 1 and 8. Adjuvant Immunotherapy: LEV - 150 mg/day for 3 days, followed by free period of 15 days.

Arm II: Chemotherapy as for Arm I. Adjuvant Immunotherapy: BCG - 6 x 10 to the eighth vial units by scarification days 1 and 8.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: 5-FU - 250 mg vials; ADR - 10 mg vials; CTX - 50 mg tablets, 200 and 1000 mg vials; MTX - 5 and 50 mg vials; VCR - 1 mg ampules; LEV - 50 mg tablets; BCG - not given.

DATE SUMMARIZED: 02/80

1.0083 LEVAMISOLE IMMUNOTHERAPY PLUS CHEMOTHERAPY WITH 5-FU/ADR/CTX FOLLOWED BY 5-FU/CTX/MTX FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) BRA-MM-GP-1001

OBJECTIVES:

I. Determine the efficacy, in terms of response, duration of remission and survival, of the combination FAC-LEV: 5-fluorouracil (5-FU)/adriamycin (ADR)/cyclophosphamide (CTX)/levamisole (LEV), followed by maintenance with intravenous CMF - 5-FU/CTX/methotrexate (MTX).

II. Determine the quantitative and qualitative toxicity of this course of treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed rapidly progressing mammary carcinoma, with measurable lesions, who have had local or regional treatment but no Chemotherapy, and who, if premenopausal, have failed to respond to hormonal therapy. Patients must have a life expectancy of more than 9 weeks, adequate bone marrow, cardiac and renal functions and no CNS metastases.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 3-Drug Combination Chemotherapy plus Immunotherapy. FAC: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; plus Levamisole, LEV, NSC-177023.

Maintenance: 3-Drug Combination Chemotherapy plus Immunotherapy. CMF: 5-FU; CTX; Methotrexate, MTX, NSC-740; plus LEV.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Biochemistry, EKG, photographs, myelogram, PPD, urine typing.

END POINTS: Response/remission rate, duration of response, survival time, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: 5-FU - 700 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; CTX - 700 mg/sqm iv on day 1; LEV - 100 mg/sqm po on days 4 through 6 and 18 through 20. Repeat course q 3 weeks if hematologic toxicity permits.

Maintenance: 5-FU - 700 mg/sqm iv on day 1; CTX - 700 mg/sqm iv on day 1; MTX - 60 mg/sqm iv on day 1; LEV - 100 mg/sqm po on days 4 through 6 and days 18 through 20. Repeat course q 3 weeks. Continue treatment for 6 months if possible.

Remove patients with progression or lack of response after 3 months from study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: 5-FU - 250 mg ampules; ADR - 10 and 50 mg ampules; CTX - 200 and 1000 mg ampules; MTX - 50 mg bottles; LEV - 80 and 150 mg tablets.

DATE SUMMARIZED: 11/78

1.0084 FAC (5-FU/ADR/CTX) CHEMOTHERAPY VS FAC PLUS IMMUNOTHERAPY WITH BCG FOR STAGE IV BREAST CARCINOMA

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PROTOCOL NUMBER(S) CAN-OCF-BR-1

OBJECTIVES:

I. Determine whether the length of remission and survival can be improved by combination chemotherapy using 5-fluorouracil, adriamycin, and cyclophosphamide, with or without BCG-Connaught.

II. Define the importance of immunologic parameters in the number and duration of remissions.

PROTOCOL ENTRY CRITERIA: Women under the age of 65 with Stage IV breast carcinoma who have failed hormonal therapy. Patients may have had prior adjuvant chemotherapy only; other prior treatments disqualify patient from entry.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Immunotherapy. FAC: Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893; plus BCG-Connaught, BCG, NSC-B116341.

Arm II: 3-Drug Combination Chemotherapy. FAC.

STRATIFICATION BY: Site and extent of metastases: widespread major organ disease, pulmonary, bone alone, ipsilateral pleura plus or minus skin, local skin and node, liver alone.

SPECIAL STUDY PARAMETERS: Pre-chemotherapy, CEA, serum ferritin, GCDFP and ClqBA.

END POINTS: Recurrence rate, length of survival.

CURRENT STATUS: 75 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: FAC: ADR - 50 mg/sqm iv q 28 days; CTX - 500 mg/sqm iv q 28 days; 5-FU - 500 mg/sqm iv q 28 days. BCG - 5 mg id by sterngun at weekly intervals for 2 months, then monthly on day 21 following the administration of Chemotherapy.

Arm II: ADR; CTX; 5-FU as in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

1.0085 CHEMOTHERAPY WITH FAC (5-FU/ADR/CTX) WITH OR WITHOUT TMX FOR DISSEMINATED STAGE IV CARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) CHILE-BR-7801

OBJECTIVES:

I. Determine whether the addition of oophorectomy improves the response rate and duration of response in premenopausal patients with disseminated breast carcinoma.

II. Determine whether the addition of tamoxifen (TMX) to FAC - 5-fluorouracil (5-FU)/cyclophosphamide (CTX)/adriamycin (ADR) - improves the response rate and duration of response in disseminated breast carcinoma in postmenopausal patients.

III. Determine the toxicity associated with the addition of TMX to the FAC regimen.

PROTOCOL ENTRY CRITERIA: Patients under 70 years old with histologically proven, measurable, Stage IV carcinoma of the breast who are not known to be refractory to 5-FU, methotrexate or ADR. Patients must have recovered from toxicity associated with prior therapy and be off therapy for 4 weeks prior to entry. Patients must have adequate bone marrow and cardiac status and no CNS metastases.

PROTOCOL OUTLINE: Randomized study.

Arm I: Induction: 3-Drug Combination Chemotherapy. FAC: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Maintenance: 3-Drug Combination Chemotherapy. CMF: CTX, 5-FU; Methotrexate, MTX, NSC-740.

Arm II: Induction: 3-Drug Combination Chemotherapy plus Antiestrogen Therapy. FAC; Tamoxifen, TMX, NSC-180973.

Maintenance: 3-Drug Combination Chemotherapy plus Antiestrogen Therapy. CMF; TMX.

STRATIFICATION BY: Participating institutions; menopausal status; disease free interval: less than 12 months vs. 13 to 60 months vs. over 61 months; number of organ sites involved: 1 or 2 vs. 3 or more; dominant site: visceral vs. osseous vs. soft tissue.

SPECIAL STUDY PARAMETERS: Liver and bone scans.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, duration of survival, objective tumor response.

CURRENT STATUS: 150 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Induction: FAC: 5-FU - 500 mg/sqm iv on days 1 and 8; ADR - 40 mg/sqm iv on day 1; CTX - 500 mg/sqm iv on day 1. Repeat course q 21 days for 10 courses.

Maintenance: CMF: CTX - 600 mg/sqm iv on day 1; MTX - 30 mg/sqm iv or im on days 1 and 8; 5-FU - 400 mg/sqm iv on days 1 and 8. Repeat course q 21 days.

Arm II: Induction: FAC as in Arm I; TMX - 20 mg/day po in 2 divided doses. Repeat course q 21 days for 10 courses.

Maintenance: CMF as in Arm I; MTX as in Induction.

Remove from study patients with progressive disease after 2 courses of Induction, patients in complete remission, or for unacceptable toxicity or status quo.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; ADR - 10 and 50 mg ampules; CTX - 100 and 500 mg ampules; MTX - 5 and 50 mg vials; TMX - not given.

DATE SUMMARIZED: 12/78

1.0086 APD CHEMOTHERAPY FOR OSTEOLYTIC BONE DISEASE DUE TO BREAST CANCER

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PROTOCOL NUMBER(S) DUT-APD-BR-2

OBJECTIVES:

I. Assess the efficacy and safety of APD in osteolytic bone disease due to breast cancer.

PROTOCOL ENTRY CRITERIA: Female patients with histologically proven progressive metastatic bone disease due to breast cancer. Patients must not be receiving chemotherapy for their disease 3 weeks before and 6 weeks after start of APD administration; they must not be receiving radiotherapy unless they have at least one nonirradiated evaluable bone lesion. Patients must not be in a preterminal or cachectic state or be on any other trial acting on tumor cells or calcium metabolism. They must have a creatinine clearance of less than 30 ml/minute.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. APD - 3-amino-1-hydroxypropane-1, 1-diphosphonic acid, no NSC available.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Calcium/creatinine ratio, hydroxyproline/creatinine ratio, TMP/GFR ratio, bone scans, iliac crest biopsy.

END POINTS: Progression of osteolytic lesions, changes in pain scale, decrease in urinary calcium and hydroxyproline output, changes in bone scan and X-ray, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 25 patients will be entered.

DOSAGE SCHEDULE:

APD - 11.2 mg/kg/day po given in 3 divided doses before meals on days 1 through 5, then 5.6 mg/kg/day for a minimal total of 3 weeks and preferably for 6 weeks.

DOSAGE FORMS: APD capsules.

DATE SUMMARIZED: 09/79

1.0087 DOUBLE-BLIND EVALUATION OF IMMUNOTHERAPY WITH LEVAMISOLE FOLLOWING RADICAL MASTECTOMY AND RADIOTHERAPY FOR BREAST CANCER

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PROTOCOL NUMBER(S) DUT-LEVAM-RRTI

OBJECTIVES:

I. Evaluate in a double-blind trial adjuvant immunotherapy with levamisole following radical mastectomy and radiotherapy in patients with Stage II breast cancer.

II. Study the effects of levamisole on lymphocytes (K cell cytotoxicity).

PROTOCOL ENTRY CRITERIA: Patients with Stage II breast cancer that has been treated by radical or modified radical mastectomy and postoperative radiotherapy. Patients may not have a second malignancy or rheumatic disease and must not be over the age of 75.

PROTOCOL OUTLINE: Randomized, double-blind study.

Arm I: Immunotherapy. Levamisole, LEV, NSC-177023.

Arm II: Placebo.

STRATIFICATION BY: Age, hormonal status, nodal status, hormone receptor status, menopausal status, histology.

SPECIAL STUDY PARAMETERS: Immunologic parameters, K cell cytotoxicity.

END POINTS: Disease-free interval, recurrence rate, survival, immunological status.

CURRENT STATUS: About 200 patients will be entered.

DOSAGE SCHEDULE:

Arm I: LEV - dosage according to weight: less than 50 kg, 100 mg; 51-70 kg, 150 mg; 71-90 kg, 200 mg; over 90 kg, 250 mg. Administer po on 2 consecutive days of each week for 2 years.

Arm II: Placebo.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: LEV - 50 mg tablets.

DATE SUMMARIZED: 01/81

1.0088 CMF (CTX/MTX/5-FU) THERAPY FOLLOWING RADIOTHERAPY AND MASTECTOMY FOR PATIENTS WITH BREAST CANCER AND AXILLARY METASTASES

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PROTOCOL NUMBER(S) EORTC-09771

OBJECTIVES:

I. Determine the effectiveness of postoperative chemotherapy with cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU)/in relation to: 1. the duration of the clinically detectable metastatic free interval, and 2. survival in breast cancer patients (irrespective of their menstrual activity), who, having received intended curative surgery, were found to have axillary but not infraclavicular (axilla top) metastases for which they were shortly afterwards irradiated.

PROTOCOL ENTRY CRITERIA: Patients, under 70 years of age, who have undergone curative mastectomy (radical or modified radical) for histologically proven carcinoma of the breast, classified T1a T2a T3a N0N1M0, with one or more involved lymph nodes, not including the highest infraclavicular lymph node. Patient must not have had prior therapy and must not have distant metastases. Patients must have normal alkaline phosphatase or other liver function tests, normal hematologic status, and diagnostic biopsy must have been performed within 4 weeks of surgery.

PROTOCOL OUTLINE: Randomized study. Following radiotherapy, randomize patients to Arms I or II.

Radiotherapy-240 KEV X-rays or 10 MEV electrons. To patients with 1 to 3 lymph node metastases give parasternal radiotherapy; irradiate all regional lymph node areas for patients with 4 or more positive lymph nodes.

Chemotherapy:

Arm I: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Control. No Chemotherapy.

STRATIFICATION BY: Menopausal status, nodal status.

SPECIAL STUDY PARAMETERS: Liver function tests, skeletal survey, mammography.

END POINTS: Disease-free interval, survival time.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Radiotherapy: Enter all patients 4 to 6 weeks following surgery. Parasternal: 3500 to 4000 rad given in 3 to 4 weeks to homolateral lymph nodes. Regional lymph nodes: 4500 to 5000 rad in 4.5 to 5 weeks to supraclavicular axillary lymph nodes. Maximum total radiotherapy time is 6 weeks.

Chemotherapy: Enter patients 7 to 10 days following completion of radiotherapy or upon hematologic recovery.

Arm I: CTX - 50 mg/sqm/day po on days 1 through 14; MTX - 15 mg/sqm iv on days 1 and 8; 5-FU - 350 mg/sqm iv on days 1 and 8. Repeat therapy on day 20 and q 4 weeks for 24 months, or until prior recurrence or metastases or unacceptable toxicity.

Arm II: No further therapy.

Follow up all patients q 3 months for 5 years, except that patients with 1-3 involved nodes, who are free of recurrences at 3 years, may be followed q 6 months for the next 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 5 mg tablets; 5-FU - 250 mg ampules; MTX - 5 and 50 mg ampules.

DATE SUMMARIZED: 05/79

1.0089 POSTOPERATIVE CHEMOTHERAPY WITH CTX/5-FU/MTX PLUS IMMUNOTHERAPY WITH LEVAMISOLE PLUS RADIOTHERAPY FOR PRIMARY BREAST CARCINOMA

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PROTOCOL NUMBER(S) EORTC-10761

OBJECTIVES:

I. Assess the efficacy of immunotherapy for primary breast cancer with positive axillary nodes, with regard to (a) length of disease-free interval, (b) length of survival, and (c) undesirable side effects.

PROTOCOL ENTRY CRITERIA: Female patients, under 65 years of age, with histologic proof of primary breast cancer with positive axillary nodes. Patients must not have distant metastasis or additional primaries, or have undergone prior therapy other than surgery.

Patients must undergo total mastectomy including total 'en bloc' axillary dissection within four weeks of entry.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus 3-Drug Combination Chemotherapy plus Immunotherapy. Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740; Levamisole, LEV, NSC-177023; Radiotherapy to internal mammary nodes.

Arm II: Radiotherapy plus 3-Drug Combination Chemotherapy plus Placebo. CTX; 5-FU; MTX; plus placebo. Radiotherapy as in Arm I.

STRATIFICATION BY: Participating institutions; high risk or low risk; nodal involvement.

SPECIAL STUDY PARAMETERS: Skeletal X-ray, EPA chest X-ray, bone scan, skin tests, immunoglobulins.

END POINTS: Toxicity/morbidity of treatment, length of disease-free interval, length of survival, recurrence rate, rate of metastasis.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Radiotherapy: Deliver 4000 rads at 3 cm depth within 3 weeks (megavolt) or 3350 rads at 3 cm depth within 3 weeks (orthovolt) to internal mammary nodes from 2 cm above the sternal notch down to the fifth intercostal space. Start Radiotherapy within 4 weeks of Surgery. Chemotherapy begins at the same time as Radiotherapy. (Within maximum delay of 6 weeks postop) CTX - 100 mg/sqm, po, for days 1 through 14; 5-FU - 600 mg/sqm, iv, on days 1 and 8; MTX - 40 mg/sqm, iv, on days 1 and 8. Repeat course q 28 days until the patient has received 12 courses, after which no further treatment is to be given unless there is a relapse. Immunotherapy begins on day 14 of the 1st Chemotherapy course. LEV - 2.5 mg/kg/day for 2 consecutive days once a week for a period of 2 years. Patients with recurrence or metastasis during the therapy go off study.

Arm II: Radiotherapy: same as in Arm I. Chemotherapy: same as in Arm I. Placebo tablets instead of LEV; give as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: LEV - 50 mg tablets; CTX, 5-FU and MTX - none given.

DATE SUMMARIZED: 12/78

PATIENT ACCRUAL: 01760177

1.0090 CMF VS CMF/TAMOXIFEN IN POSTMENOPAUSAL WOMEN WITH ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) EORTC-10762

OBJECTIVES:

I. Determine the benefit of the addition of tamoxifen to standard combination chemotherapy with cyclophosphamide, 5-fluorouracil and methotrexate (CMF) in advanced breast cancer.

PROTOCOL ENTRY CRITERIA: All postmenopausal women up to 68 years of age (or all up to 75 years of age in any one institution) with breast cancer. Patients must have adequate wbc, platelet, creatinine and calcium levels, must have a grade 2 performance status or better. Toxic manifestations of prior Radiation, Hormonal Therapy or Chemotherapy, which must not have been with the study agents, must have been resolved. Progressive disease must be evident if prior therapy has been given.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. CFM: Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. CFM-TAM: CTX; 5-FU; MTX; as in Arm I, plus Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of remission, duration of survival, objective tumor response.

CURRENT STATUS: 180 patients will be entered.

DOSAGE SCHEDULE:

Arm I: CTX - 100 mg/sqm po on days 1 through 14; 5-FU - 600 mg/sqm iv on days 1 and 8; MTX - 40 gm/sqm iv on days 1 and 8. Monitor complete blood counts before each iv dose on days 1 and 8.

Arm II: CTX; 5-FU; MTX; as in Arm I; plus TMX - 40 mg/day po in 2 divided doses. Monitor cbc as in Arm I.

Evaluate all patients to determine response to therapy by the 17th week. Repeat courses in Arms I and II q 28 days, unless delay is necessary to allow for hematologic recovery. Continue therapy for a minimum of 8 weeks until progression or reactivation of disease.

Dosage modifications for toxicity and for patients above age 68 are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/79

PATIENT ACCRUAL: 02151078

1.0091 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED RECURRENT OR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) EORTC-10791

OBJECTIVES:

I. Assess the objective antitumor activity of PALA in patients with advanced breast cancer previously treated with conventional chemotherapy.

II. Characterize further the toxic effects of PALA.

PROTOCOL ENTRY CRITERIA: Patients with histological evidence of recurrent or metastatic breast cancer, with objective evidence of progressive disease. Clinical disease must be evaluable by direct measurement or photography and/or radiography. Patients must be no older than 70 years of age. The Karnofsky performance status must be at least 50; life expectancy must be at least 3 months, and hematologic, renal, and hepatic function must be adequate. Patients must not have CNS metastases, previous or current malignancies at other sites (except cone biopsied in situ carcinoma of the cervix uteri and adequately treated basal or squamous cell carcinoma of the skin), uncontrolled infection, or nonmalignant systemic disease. All anticancer treatments must have been withdrawn for at least 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests, renal and hepatic function tests, assessment of palpable lesions, chest x-rays, bone survey, photographs of all visible lesions.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: Initially, 20 patients will be treated; 5 patients will be added for each response seen..

DOSAGE SCHEDULE:

PALA - 2.5 g/sqm iv infusion over 60 minutes on days 1 and 2 q 2 weeks. All patients showing response continue treatment until tumor progression. Patients showing no change after 6 courses go off study. Patients who develop severe toxicity, despite 50 percent dose reduction, go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 1 g ampules.

DATE SUMMARIZED: 10/80

1.0092 COMBINATION CHEMOTHERAPY WITH CMF (CTX/MTX/5-FU) AND/OR ENDOCRINE THERAPY WITH PRDL OR TMX ADDED TO PRIMARY RADIOTHERAPY FOR BREAST CANCER

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PROTOCOL NUMBER(S) EORTC-10792

OBJECTIVES:

I. Test, in a prospective randomized clinical trial, the contribution of both cytotoxic chemotherapy with CMF (cyclophosphamide/methotrexate/5-fluorouracil) and endocrine therapy with prednisolone or tamoxifen to the primary treatment of locally-advanced breast cancer by radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed locally-advanced breast cancer characterized by one or more of the following features: oedema of more than one-third of the skin over the breast, satellite tumor nodules in the skin of the affected breast, diffuse carcinoma, fixation of the tumor to underlying chest wall, skin infiltration greater than the diameter of the tumor, skin ulceration not associated with Paget's disease of the nipple, oedema of the arm, attachment of axillary lymph nodes to skin or chest wall, and histologically confirmed involvement of supra-clavicular or infra-clavicular or internal mammary nodes. Patients must not have received previous operative, systemic or radiation treatment for breast cancer. Patients must not be pregnant, be currently receiving systemic corticosteroid therapy, or have previous or concomitant malignancy (except treated squamous or basal-cell carcinoma of the skin or carcinoma in situ of the cervix). Patients between 45 and 55 years of age who have had a hysterectomy with one or both ovaries retained are excluded. Patients must be physically and mentally fit for any of the protocol treatment options.

PROTOCOL OUTLINE: Randomized study. Patients showing CR or PR after Radiotherapy are randomized to Arms I, II, III and IV.

Regimen A: Radiotherapy. Supervoltage.

Arm I: Endocrine Therapy. Premenopausal patients: Prednisolone, PRDL, NSC-9900. Postmenopausal patients: Tamoxifen, TMX, NSC-180973. Premenopausal patients also receive additional Radiotherapy.

Arm II: 3-Drug Combination Chemotherapy. CMF: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm III: 3-Drug Combination Chemotherapy plus Endocrine Therapy. CMF: CTX; MTX; 5-FU; plus TMX (postmenopausal) or PRDL (premenopausal).

Arm IV: No further treatment.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; mammography; chest radiograph and lateral view; radiological skeletal survey; biopsy; tumor measurements.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, disease-free interval, survival rate, length of survival, objective tumor response.

CURRENT STATUS: Approximately 60 patients per year will be entered.

DOSAGE SCHEDULE:

Regimen A: Supervoltage radiation - 4600 rads in 23 daily fractions within 5 weeks; immediately thereafter, give booster dose of 1400 rads in 200-rad daily fractions over 7 days.

Arm I: Postmenopausal patients: PRDL - 7.5 mg in 3 equal doses per day for 5 years; plus supervoltage irradiation - 1500 rads ovarian irradiation in 5 consecutive days. Premenopausal patients: TMX - 20 mg in 2 equal doses per day for 5 years.

Arm II: CMF: CTX - 100 mg/sqm (maximum 150 mg) po daily on days 1 to 14; MTX - 30 mg/sqm (maximum 50 mg) iv on days 1 and 8; plus 5-FU - 600 mg/sqm iv on days 1 and 8. Repeat cycle on day 29 for 8 courses.

Arm III: CMF: CTX; MTX; 5-FU as in Arm II plus TMX or Radiotherapy plus PRDL as in Arm I.

Arm IV: No further treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

1.0093 RADIOTHERAPY AND ADJUVANT CTX/5-FU/MTX/TMX FOLLOWING RADICAL OR LIMITED SURGERY FOR BREAST CARCINOMA

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PROTOCOL NUMBER(S) EORTC-10801

OBJECTIVES:

I. Determine the results of breast-conserving therapy (radiotherapy plus surgery) for operable breast cancer with regard to survival, length of disease-free period, and quality of life (cosmetic results, psychologic factors, functional tests of arm movements).

PROTOCOL ENTRY CRITERIA: Patients with Stage I or II histologically proven breast carcinoma; axillary lymph node metastases must either be absent or operable. Patients must be less than 68 years of age and have a Karnofsky performance index of 80 or greater. There must not be other malignant tumors except nonmelanomatous skin tumors. Patient must be accessible for prolonged follow-up.

PROTOCOL OUTLINE: Randomized study. Patients with histological proof of axillary node involvement also receive Adjuvant Therapy.

Arm I: Surgery plus Radiotherapy. Radical mastectomy; plus parasternal field and axillary field megavoltage irradiation.

Arm II: Surgery plus Radiotherapy. Lumpectomy; plus external megavoltage irradiation of the breast and booster tumor bed irradiation by Iridium implants.

Adjuvant Therapy: 3-Drug Combination Chemotherapy plus Hormone Therapy. CMF: Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740; plus Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Participating institutions, disease stage, menopausal status.

SPECIAL STUDY PARAMETERS: Psychological and social state, tracer isotopes for skeletal and internal mammary lymph node scans, CT and/or ultrasound scans of chest, photography of both breasts in 3 positions.

END POINTS: Toxicity/morbidity of treatment, disease-free interval, length of survival.

CURRENT STATUS: Up to 450 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Radical mastectomy - en bloc breast-axilla resection by a standard Halsted or Patey procedure. Beginning as soon as possible (within 6 weeks) after Surgery, patients with centrally or medially localized tumors, or lateral tumors with lymph node metastases in the axilla receive 450 rads in 5 weeks at 3-cm depth to the parasternal lymph node region (those with a pathologic lymph node scan receive a booster dose of 150 rads given with electrons. Irradiation of the axilla, 450 rads in 5 weeks encompassing the supra- and subclavicular nodes and the axilla, is given in case of surgical errors indicating the risk of contamination of the axillary field.

Arm II: Lumpectomy - local excision of tumor, excising a 1-cm margin of normal looking breast tissue plus axillary dissection - total clearance of all axillary nodes with preservation of muscle and long thoracic nerve. For tumors localized in upper outer quadrant of the breast, en bloc removal of upper outer quadrant and axillary contents is performed. Beginning as soon as possible (within 6 weeks) after Surgery, Radiotherapy (450 rads in 5 weeks, with a daily dose of 18 rads) is administered to the whole breast. Radiotherapy to the parasternal lymph node and axillary regions is given as in Arm I. After healing of the skin, and within 2 to 6 weeks after completion of external radiation, booster therapy (Iridium implantation) is done. Implantation should be done in two planes, with the target volume including the whole excisional bed with 1-cm margin (2 cm for microscopic irradical lumpectomy) and the efferent mammary ducts from the tumor bed to the nipple. Dose is calculated by the Paris system (details in protocol). Patients with tumors in the upper outer quadrant of the breast undergoing en bloc upper outer quadrant removal receive an extra dose of 10 rads external irradiation to the breast and no Iridium implant.

Adjuvant Therapy: CMF therapy begins one week after Surgery; courses are given every 28 days. Between course 1 and 2 there is a 6-week interval during which external irradiation (on Arm I or Arm II) is given. CMF: CTX - 100 mg/sqm po on days 1-14; 5-FU - 600 mg/sqm iv on days 1 and 8; MTX - 30 mg/sqm iv on days 1 and 8; TMX - 20 mg daily in 2 divided doses for the duration of Chemotherapy. Booster Radiotherapy on Arm II is given on day 50 following Surgery.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

1.0094 PHASE II CHEMOTHERAPY WITH ADRIAMYCIN, CARMINOMYCIN AND QUELAMYCIN FOR ADVANCED BREAST CANCER

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PROTOCOL NUMBER(S) EORTC-16802

OBJECTIVES:

I. Determine the antitumor activity of carminomycin and quelamycin given to patients with advanced breast cancer previously treated with conventional chemotherapy.

II. Compare the toxicity of these compounds and their cross resistance with adriamycin.

PROTOCOL ENTRY CRITERIA: Patients with histological evidence of recurrent metastatic breast cancer that is progressive. All prior conventional therapies except anthracycline are allowed if treatments were withdrawn for at least 4 weeks prior to entry and no toxic manifestations are evident. Patients must be no older than 70 years of age; Karnofsky index must be equal to or greater than 50. Patients must have a minimum life expectancy of 3 months. Adequate blood counts and renal and hepatic funcion are required. There must have been no severe cardiac disease within the 4 months prior to entry; there must be no present or prior malignancies at other sites.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Carminomycin, NSC-180024.

Arm II: Single-agent Chemotherapy. Quelamycin.

STRATIFICATION BY: Participating institutions; age: less vs. more than 50 years; dominant disease status: soft tissue vs. visceral; performance status: less vs. more than 80.

SPECIAL STUDY PARAMETERS: Echocardiogram; liver, brain, and bone scans; bone survey; hematologic, renal, and hepatic function tests.

END POINTS: Toxicity/morbidity of treatment, duration of response, length of survival.

CURRENT STATUS: 40-50 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Carminomycin - 20 mg/sqm rapid iv injection q 3 weeks for a minimum of 2 courses. If partial (PR) or complete (CR) remission, or no change (NC), continue treatment; if disease progresses, change to ADR - 75 mg/sqm iv q 3 weeks to maximum total dose of 400 mg/sqm.

Arm II: Quelamycin - 150 mg/sqm rapid iv injection q 3 weeks for a minimum of 2 courses. If PR, CR or NC, continue treatment; if progressive disease, change to ADR as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Carminomycin - 10 mg vials; Quelamycin - 25 mg vials; ADR - 10 and 100 mg vials.

DATE SUMMARIZED: 10/80

1.0095 PHASE II CHEMOTHERAPY WITH ADR/DAVA FOR METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) GER-GO-MC-IV/80

OBJECTIVES:

I. Determine the therapeutic efficacy of adriamycin and vindesine as primary treatment of patients with poor-risk, metastatic breast cancer.

II. Evaluate, in a pilot study, the optimal dose of vindesine.

PROTOCOL ENTRY CRITERIA: Patients with metastatic breast cancer at poor risk who have not been previously treated with cytostatics. There must be no concurrent hormone treatment.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Vindesine, DAVA, NSC-245467; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic, kidney, and liver function tests; tumor measurements.

END POINTS: Response/remission rate, duration of remission, toxicity/morbidity of treatment.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 3 mg/sqm iv q 3 weeks with possibility of dosage increase of 1 mg/sqm upon consultation with study chairman; ADR - 60 mg/sqm iv q 3 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 01/81

1.0096 COMBINATION CHEMOTHERAPY WITH CTX/VCR/ADR AND CTX/MTX/5-FU PLUS IMMUNOTHERAPY WITH C. PARVUM FOR BREAST CANCER

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PROTOCOL NUMBER(S) GER-OSAKO-1177

OBJECTIVES:

I. Determine the effects of various routes and timing in the administration of Corynebacterium parvum (C. parvum) with cyclophosphamide (CTX)/vincristine (VCR)/adriamycin (ADR) and cyclophosphamide/methotrexate (MTX)/5-fluorouracil (5-FU).

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with histologically proven, advanced breast cancer without prior treatment with the agents used in this study, and with normal hematologic and biochemical status.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Immunotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; plus Corynebacterium parvum, C. parvum, no NSC number, given iv on day 1 concurrent with drugs.

Arm II: 3-Drug Combination Chemotherapy plus Immunotherapy. ADR; CTX; VCR; plus C. parvum iv on day 14 sequentially.

Arm III: 3-Drug Combination Chemotherapy plus Immunotherapy. ADR; CTX; VCR; plus C. parvum sc on day 1 concurrently.

Arm IV: 3-Drug Combination Chemotherapy plus Immunotherapy. ADR; CTX; VCR; plus C. parvum sc on day 14 sequentially.

Upon completion of six 28-day cycles, the following drugs will replace ADR and VCR in a repeat of the foregoing therapies: 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740.

STRATIFICATION BY: Menopausal status, prior therapy, site of metastases.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: 141 patients will be entered.

DOSAGE SCHEDULE:

Arm I: ADR, CTX, VCR (dosages not given) q 28 days for 6 cycles, then CMF: CTX, MTX, 5-FU q 28 days; C. parvum iv on day 1 of each cycle.

Arm II: ADR, CTX, VCR and CTX, MTX, 5-FU as in Arm I; C. parvum iv on day 14 of each cycle.

Arm III: ADR, CTX, VCR and CTX, MTX, 5-FU as in Arm I; C. parvum sc on day 1 of each cycle.

Arm IV: ADR, CTX, VCR and CTX, MTX, 5-FU as in Arm I; C. parvum sc on day 14 of each cycle.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

1.0097 ADJUVANT CHEMOTHERAPY WITH CMF AND AV COMBINATIONS, DBD, HMM, MITO AND HORMONE THERAPY WITH TMX/MPA FOR BREAST CANCER IN PREMENOPAUSAL WOMEN

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PROTOCOL NUMBER(S) ITA-MIL-7802

OBJECTIVES:

I. Assess in premenopausal women with operable breast cancer the value of new prognostic discriminants other than the number of axillary lymph nodes when patients are treated with 12 cycles of adjuvant CMF: cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU).

II. Test the therapeutic effects of surgical castration in patients relapsing after radical mastectomy plus CMF.

III. Test the therapeutic effects of AV: adriamycin (ADR)/vincristine(VCR) after primary ovariectomy failure or subsequent relapse.

PROTOCOL ENTRY CRITERIA: Premenopausal patients with breast cancer having 1 or more tumor positive axillary nodes after radical or modified radical mastectomy. Patients must have tumor more than 2 cm in diameter and axillary nodes which are nonpalpable or moveable in relation to the chest wall or neurovascular bundle. Patients must have adequate renal and bone marrow function and must have had no prior breast cancer treatment. Patients must have postsurgical staging T2a-T3a, N plus with a unilateral malignancy and may not be pregnant or lactating.

PROTOCOL OUTLINE: Nonrandomized study.

Induction:

Regimen A: Enter all patients 2-4 weeks following mastectomy. 3-Drug Combination Chemotherapy. CMF: Cyclophosphamide, CTX, NSC-26271, Methotrexate, MTX, 5-Fluorouracil, 5-FU, NSC-19893.

Regimen B: Enter all patients in relapse following Induction Chemotherapy. Surgical Therapy. Ovariectomy.

Regimen C: Enter all patients with progressive disease or in relapse. 2-Drug Combination Chemotherapy. AV: Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574.

Regimen D: Enter patients refractory to AV or when cumulative dose of ADR totals 550-600 mg/sqm and estrogen receptor negative. Single-agent Chemotherapy. Dibromodulcitol, DBD, NSC-104800.

Regimen E: Enter patients as in Regimen D. Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

Regimen F: Enter patients as in Regimen D. Single-agent Chemotherapy. Mitomycin C, MITO, NSC-26980.

Regimen G: Enter patients refractory to AV or when cumulative dose of ADR totals 550-600 mg/sqm and estrogen receptor positive. 2-Drug Combination Hormone Therapy. Tamoxifen, TMF, NSC-180973; Medroxyprogesterone Acetate, MPA, NSC-26386.

STRATIFICATION BY: Estrogen receptor, resistance to specific drugs, (AV), disease stage.

SPECIAL STUDY PARAMETERS: Hepatic, renal and bone function; vaginal hormonal cytology; Schiller test; serum tumor markers; estrogen receptor studies; cell kinetics studies (labelling index); whole body and liver scans.

END POINTS: Response/remission rate, survival time, disease free interval.

CURRENT STATUS: At least 100-150 patients will be entered in about 1 1/2 years.

DOSAGE SCHEDULE:

Induction:

Regimen A: CMF: CTX - 100 mg/sqm po on days 1 through 14; MTX -40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8. Repeat q 28 days for 12 courses or until disease progresses. After 12 courses complete responders receive no further therapy. Nonresponders enter Regimen B.

Regimen B: Surgical Therapy. Ovariectomy. Evaluate patients 8 weeks after surgery. Nonresponders or patients with progressive disease or in later relapse enter Regimen C. Follow-up responders at least 4 years.

Regimen C: ADR - 60 mg/sqm iv on day 1 (maximum cumulative dose 550-600 mg/sqm); VCR - 1.4 mg/sqm iv on days 1 and 8. Repeat course q 21 days. Continue course until maximum ADR dose or refractory state. Then enter patients with negative estrogen receptor status in either Regimen D, E or F. Estrogen receptor positive patients enter Regimen G.

Regimen D: DBD - 140 mg/sqm po on days 1 through 10. Repeat q 28 days.

Regimen E: HMM - 300-400 mg/sqm po on days 1 through 17. Repeat q 28 days.

Regimen F: MITO - 10-15 mg/sqm iv day 1. Repeat q 4 to 6 weeks upon bone marrow recovery.

Regimen G: TMX - 20 mg/day po; MPA - 500 mg im 3 times per week. Follow-up all patients at least 4 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 50 mg tablets; 5-FU - 250 mg vials; MTX - 5 and 50 mg vials; ADR - 10 mg vials; VCR - 1 mg ampules; DBD - 50 and 100 mg tablets; HMM - 50 and 100 mg (container not given); MITO - 2 mg vials; TMX - 10 mg tablets; MPA - 500 and 100 mg ampules.

DATE SUMMARIZED: 10/78

1.0098 PHASE II CHEMOTHERAPY WITH PROCARBAZINE FOR RECURRENT OR METASTATIC ADENOCARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) PERU-INEN-7801

OBJECTIVES:

I. Determine the response rate and duration of response of patients with breast cancer to treatment with procarbazine.

PROTOCOL ENTRY CRITERIA: Patients with measurable recurrent or metastatic histologically proven adenocarcinoma of the breast who have failed on standard chemotherapy. Patients may not have had prior exposure to PCB, must have a performance status of 3 or less and adequate bone marrow function.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: Single-agent Chemotherapy. Procarbazine, PCB, NSC-77213.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Objective tumor response, response/remission rate, duration of response.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

Induction: PCB - 33 mg/sqm/day po on days 1 through 21. Repeat course q 29 days for a minimum of 2 courses, then remove patients with disease progression from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/78

1.0099 CMF (CTX/MTX/5-FU) PLUS SURGERY AND/OR RADIOTHERAPY PLUS LEVAMISOLE IMMUNOTHERAPY FOR STAGE III CANCER OF THE BREAST

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PROTOCOL NUMBER(S) PERU-INEN-7804

OBJECTIVES:

I. Evaluate whether adjuvant chemotherapy with CMF: cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU) before, during and after surgery or radiotherapy reduces the recurrence rate as compared with our results in PERU-INEN-7401.

II. Evaluate whether surgery followed by radiotherapy reduces the recurrence rate and improves the survival in this group of patients as compared with radiotherapy and CMF.

III. Evaluate whether nonspecific immune manipulation with levamisole (LEV) reduces recurrence and improves survival as compared to no immunotherapy.

IV. Compare CMF plus radiotherapy versus CMF plus surgery followed by postoperative radiotherapy in these patients.

PROTOCOL ENTRY CRITERIA: Previously untreated patients under 80 years of age with biopsy confirmed Stage III unilateral carcinoma of the breast. Patients must not have cardiovascular disease, liver failure or neuropsychiatric disorders. Patients must have adequate bone marrow, liver and kidney function, and must not be pregnant or within 6 months postpartum.

PROTOCOL OUTLINE: All patients enter Induction. Following Induction, patients are randomized to Arms I and II. After therapy on Arm I or Arm II, patients are rerandomized to Arms III and IV.

Induction: 3-Drug Combination Chemotherapy. CMF: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

Arm I: 3-Drug Combination Chemotherapy plus Radiotherapy. CMF plus Cobalt-60 supervoltage Radiotherapy.

Arm II: Surgery plus 3-Drug Combination Chemotherapy plus Radiotherapy. CMF.

Arm III: 3-Drug Combination Chemotherapy plus Immunotherapy. CMF plus Levamisole, LEV, NSC-177023.

Arm IV: 3-Drug Combination Chemotherapy. CMF.

STRATIFICATION BY: Participating institutions; age: under 50 vs. over 50; tumor: fixed to fascia or extension to skin vs. none.

SPECIAL STUDY PARAMETERS: Bone and liver scans, mammography, serial biopsies.

END POINTS: Recurrence rate, disease free interval, survival time.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: CTX - 100 mg/sqm po on days 1 through 14; MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8.

Randomize patients on day 21 to Arm I or II.

Arm I: Radiotherapy - begin 3 to 4 weeks after the start of Induction Chemotherapy - 6000 rad in 6 1/2 weeks to the breast and 5000 rad in 5 weeks to the axilla, plus 1500 rad in 2 weeks to the primary if over 3 cm, 1000 rad in 1 week to axillary node if over 2 cm, 4500 rad to the supraclavicular area and 4500 rad to the internal mammary chain if the tangent rad fields to the breast are separated by 18 cm or more. Resume CMF therapy, as in Induction, 3 to 4 weeks after completion of Radiotherapy. Repeat course q 29 days for 6 months, then rerandomize patients to Arm III or IV.

Arm II: Total mastectomy plus lower axillary lymph node dissection 21 to 28 days after initiation of Induction therapy. 2 weeks after Surgery, administer CMF for 1 course, 3 to 4 weeks after Surgery administer Radiotherapy - 5000 rad in 6 weeks to tumor and chest wall, 4500 rad to the axilla, supraclavicular area and the internal mammary chain. After completion of Radiotherapy, resume CMF q 29 days for 6 months, then rerandomize patients to Arm III or IV.

Arm III: CMF, as in Induction q 29 days, plus LEV - 90 mg/sqm po on days 1 and 2 q 7 days for 1 year.

Arm IV: CMF as in Induction q 29 days for 1 year.

Remove all patients from protocol upon disease progression. Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 50 mg tablets, 100, 200, 500, 1000 mg vials; MTX - 2.5 mg tablets, 50, 500, 1000 mg vials; 5-FU - 500 mg ampules; LEV - 50 mg tablets.

DATE SUMMARIZED: 12/78

1.0100 CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE ADJUVANT TO RADICAL MASTECTOMY FOR PRIMARY OPERABLE BREAST CARCINOMA

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PROTOCOL NUMBER(S) UICC-73047

OBJECTIVES:

I. Determine the efficacy of chemotherapy with cyclophosphamide adjuvant to radical mastectomy for primary operable breast cancer.

PROTOCOL ENTRY CRITERIA: Patients with primary operable mammary carcinoma, Stages 1, 2 and 3. Patients over age 70 or with prior malignancies are excluded.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radical Mastectomy.

Arm II: Radical Mastectomy plus Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: Stage: 1, 2, or 3; axillary node involvement: 0, 1-2, 3-7, 8 or more.

SPECIAL STUDY PARAMETERS: Skeletal survey, detection of liver and soft-tissue metastases.

END POINTS: Response/remission rate, survival rate, duration of survival, objective tumor response, recurrence rate, appearance of metastases.

CURRENT STATUS: 150 patients will be entered per year.

DOSAGE SCHEDULE:

Arm I: Radical Mastectomy.

Arm II: Radical Mastectomy, plus CTX - 150 mg/day for 34 days beginning on the 8th postoperative day for a total of 1500 mg.

Patients are followed q 6 months for 5 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

1.0101 ADJUVANT CHEMOTHERAPY WITH L-PAM VS CTX/MTX/5-FU FOR OPERABLE CARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) UICC-76026

OBJECTIVES:

I. Determine whether chemotherapy adjuvant to surgery may prolong the disease-free interval and may improve the survival time in patients with operable carcinoma of the breast.

II. Compare the efficacy of the single agent melphalan to combination chemotherapy with cyclophosphamide, methotrexate, and 5-fluorouracil as adjuvant chemotherapy in carcinoma of the breast.

PROTOCOL ENTRY CRITERIA: Patients who have surgically removable carcinoma of the breast with histologically proven involvement of axillary lymph nodes.

PROTOCOL OUTLINE: Randomized study.

Arm I: No therapy. Placebo only.

Arm II: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm III: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Age: 50-65 years vs. below 49 years; T and N stages of axillary lymph nodes; tumor grade (UICC classification).

SPECIAL STUDY PARAMETERS: 24-hour urine hydroxyproline estimation; estrogen and progesterone receptor studies; cell proliferation studies; psychological assessment and rehabilitation study; bone and liver scintiscans, mammography, chest x-rays, skin testing for cell-mediated immunity.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, disease-free interval between operation and relapse, psychological assessment and the value of rehabilitation.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Placebo - 0.15 mg/kg/day po on days 1 through 5 and q 6 weeks x 18 months.

Arm II: L-PAM - 0.15 mg/kg/day po on days 1 through 5 and q 6 weeks x 18 months.

Arm III: CTX - 80 mg/sqm day po on days 1 through 14; MTX - 32 mg/sqm iv on days 1 and 8; 5-FU - 480 mg/sqm iv on days 1 and 8. Rest on days 15 through 28 and repeat for 12 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

1.0102 HORMONE THERAPY WITH MEDROXYPROGESTERONE ACETATE VS OOPHORECTOMY FOR ADVANCED METASTATIC OR INOPERABLE BREAST CARCINOMA

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PROTOCOL NUMBER(S) UICC-76116; ITA-BOL-066M

OBJECTIVES:

I. Compare hormone therapy with massive doses of medroxyprogesterone acetate vs. oophorectomy for advanced metastatic or inoperable breast carcinoma.

PROTOCOL ENTRY CRITERIA: Premenopausal patients with advanced inoperable or metastatic breast carcinoma (Category A3) with disease progression. Predicted survival time must be greater than 2 months and performance status greater than 30%.

PROTOCOL OUTLINE: Randomized study.

Arm I: Bilateral Oophorectomy.

Arm II: Hormone Therapy. Medroxyprogesterone acetate, MPA, NSC-26386.

STRATIFICATION BY: Disease-free interval: greater or less than 2 years; primary site of metastases: visceral, bone, soft tissue. In case of multiple sites, visceral has precedence over bone and bone over soft tissue.

SPECIAL STUDY PARAMETERS: X-rays, bone and liver scans, bilirubin, SGOT, SGPT, alkaline phosphatase, glucose, nitrogen, creatinine, calcium, plasma sodium and potassium.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, disease-free interval, symptomatic relief.

CURRENT STATUS: 48 patients will be entered in 2-3 years.

DOSAGE SCHEDULE:

Arm I: Bilateral Oophorectomy.

Arm II: MPA - 1500 mg/kg/day on days 1 through 30. Repeat cycle q 6 months until tolerance limit or disease progression.

Patients are followed once a week during Arm II and once a month after oophorectomy (Arm I). Upon disease progression cross over patients to the opposing arm.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: MPA - 500 mg and 1000 mg vials.

DATE SUMMARIZED: 05/77

1.0103 ADJUVANT CHEMOTHERAPY WITH CTX AND ANTIESTROGEN THERAPY WITH TMX, ALONE OR COMBINED, FOR BREAST CARCINOMA

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PROTOCOL NUMBER(S) UKM-KCH-BR3

OBJECTIVES:

I. Determine whether the administration of a short course of cyclophosphamide immediately postoperatively or long-term tamoxifen or a combination of these drugs results in the delay of recurrence or in the reduction of mortality of patients treated for operable carcinoma of the breast.

PROTOCOL ENTRY CRITERIA: Women under the age of 70 with operable breast carcinoma, irrespective of nodal status. Patients must have a tumor that is clinically T1 or T2, N0, N1, M0 (Manchester Stage I or II). Nodes must be biopsied for histological examination and there must be no evidence of metastases on x-ray of chest, spine or pelvis. Patients with bilateral tumor are ineligible; the tumor must not be fixed to the underlying muscle or chest wall. There must be no ulceration, skin infiltration or peau d'orange involving more than a third of the breast. Patients whose axillary nodes demonstrate deep fixity are ineligible. Patients must have normal liver and renal function and a normal blood count including platelets. Patients must not receive concomitant hormone therapy or chemotherapy; they must not receive any hormone therapy for the 6 weeks prior to entry. Patients must not have received any previous treatment for contra-lateral breast cancer.

PROTOCOL OUTLINE: Randomized study. Patients are randomized following primary treatment, mastectomy or mastectomy plus Radiotherapy.

Arm I: Control. No further treatment.

Arm II: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm III: Single-agent Antiestrogen Therapy. Tamoxifen, TMX, NSC-180973.

Arm IV: Single-agent Chemotherapy plus Single-agent Antiestrogen Therapy. CTX; TMX.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Skeletal and chest x-rays, biopsy and histology of chest wall or regional nodes, liver scan.

END POINTS: Survival, disease-free interval, recurrence rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Patients undergo total mastectomy with axillary sampling followed by Radiotherapy for node positive cases or total mastectomy plus axillary clearance with no Radiotherapy.

Arm I: No further treatment.

Arm II: CTX - 5 mg/kg iv injections on days 1 through 6 (total of 30 mg/kg is given) beginning on the first postoperative day.

Arm III: TMX - 20 mg/day in 2 divided doses, beginning within 24 hours of Surgery. TMX is given daily for 2 years or until first confirmation of distant recurrent disease.

Arm IV: TMX as in Arm III; plus CTX as in Arm II.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

1.0104 COMPARATIVE STUDY OF SURGERY/RADIOTHERAPY WITH OR WITHOUT RICH REGIMEN FOR CARCINOMA OF THE BREAST

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PROTOCOL NUMBER(S) UKM-RI-B-1

OBJECTIVES:

I. Compare the relative effectiveness of mastectomy-radiotherapy with and without the RICH regimen consisting of chemo/immuno/radiotherapies plus surgical treatment for breast cancer.

PROTOCOL ENTRY CRITERIA: Women bearing mammary cancers of Stages 2 or 3.

PROTOCOL OUTLINE: Randomized study. Age- and stage-matched cohorts areseparately randomized.

Arm I: Surgery, Radiotherapy, Immunotherapy, 4-Drug Combination Chemotherapy plus Hormone Therapy. Mastectomy and axillary clearance; supervoltage Radiotherapy, irradiated cancer cells plus Levamisole, LEV, NSC-177023; plus Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893; Melphalan, L-PAM, NSC-8806; Methotrexate, MTX, NSC-740; plus Tamoxifen, TMX, NSC-180973.

Arm II: Surgery plus Radiotherapy. Mastectomy and axillary clearance; plus supervoltage Radiotherapy.

STRATIFICATION BY: Number of axillary nodes with metastases, age, disease stage.

SPECIAL STUDY PARAMETERS: Sequential profiles of PAM (pregnancy-associated macroglobulin), gamma GT, granulocytes, lymphocytes, platelets and tuberculin skin tests.

END POINTS: Time to recrudescence of cancer, time to death.

CURRENT STATUS: 30 patients to be entered.

DOSAGE SCHEDULE:

Arm I: Mastectomy and axillary clearance followed by routine postoperative supervoltage Radiotherapy, 4500 rads given over 28 days; plus autograft irradiated 10 x 10 to the seventh or eighth cancer cells on days 0 and 365; LEV - 150 mg 2 days/week for 2 years; plus CTX (no dose given) on the day of Surgery and on day 5 following Surgery; MTX - 25 mg on days 1 and 2; 5-FU - 250 mg po in 5-day pulses every 6 weeks for 2 years. Premenopausal patients receive radiation therapy (no details given); pre- and postmenopausal patients receive TMX - 10 mg twice daily for 2 years.

Arm II: Mastectomy and axillary clearance plus post-operative supervoltage Radiotherapy, 4500 rads in 28 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: L-PAM - 5 mg tablets; MTX - 5 and 10 mg tablets; 5-FU - 250 mg vials.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

1.0105 ADJUVANT AMINOGLUTETHIMIDE PLUS HYDROCORTISONE FOR POOR-RISK PRIMARY STAGE II BREAST CANCER

Powles, T. J., Royal Marsden Hospital, Downs Rd., Sutton SM2 5PT Surrey, United Kingdom

PROTOCOL NUMBER(S) UKM-RMH-BR-1A

OBJECTIVES:

I. Assess whether adjuvant treatment with aminoglutethimide is of benefit to patients with primary poor-risk breast cancer.

PROTOCOL ENTRY CRITERIA: Female patients under 70 years old with histologically confirmed Stage II primary breast cancer who have undergone mastectomy and uniform primary treatment with radiotherapy (4000-6000 rads). Patients must have adequate renal and hepatic function and must not be pregnant or lactating.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Antihormonal Therapy plus Hormone Therapy. Aminoglutethimide, AGT, no NSC number; plus Hydrocortisone, HC, NSC-10483.

Arm II: Control group. No therapy.

STRATIFICATION: None given.

SPECIAL STUDY PARAMETERS: Estrogen receptor assay, bone scan, biochemical markers and hormone profile.

END POINTS: Disease-free interval, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: 400 patients will be entered.

DOSAGE SCHEDULE:

Arm I: AGT - 250 mg po twice a day for 1 month, 3 times a day for the second month, then 4 times a day for 2 years; HC - 20 mg po twice a day concurrent with AGT. Follow up patients q week for 2 weeks, then q 3 months. Sequentially restage patients q 6 months, or when metastatic disease is suspected; when confirmed, discontinue therapy.

Arm II: No further therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/79

1.0106 ANTIHORMONAL THERAPY WITH AMINOGLUTETHIMIDE VS TAMOXIFEN FOR ADVANCED METASTATIC BREAST CANCER

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PROTOCOL NUMBER(S) UKM-RMH-BR-1B

OBJECTIVES:

I. Compare aminoglutethimide vs. tamoxifen in advanced breast cancer with regard to overall response rate, duration of response, and sites of response.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic breast carcinoma, not previously treated by systemic or ablative therapy. Patients must have adequate renal and cardiac function and be able to complete a minimum of 6 weeks of treatment.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Antihormonal Therapy plus Hormone Therapy. Aminoglutethimide, AGT, no NSC number; plus Hydrocortisone, HC, NSC-10483.

Arm II: Single-agent Antiestrogen Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION: None given.

SPECIAL STUDY PARAMETERS: Estrogen receptor assay, liver function tests, x-rays of osteolytic lesions, bone scan, skeletal survey.

END POINTS: Response/remission rate, response duration, sites of response.

CURRENT STATUS: 200 patients will be entered.

DOSAGE SCHEDULE:

Arm I: AGT - 250 mg po twice a day for 2 weeks, 3 times a day for 2 additional weeks, then 4 times a day for a minimum of 6 weeks; HC - 20 mg po twice a day concurrent with AGT. Continue therapy until relapse or disease progression.

Arm II: TMX - 20 mg/day (route not given) for a minimum of 6 weeks. Continue therapy until relapse or disease progression.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/79

SECTION 2

GASTROINTESTINAL TUMORS

2A. ESOPHAGUS

EST-PB-279	PILOT STUDY OF CHEMOTHERAPY WITH MTX/BLM/METHYL-GAG/CIS-PLATINUM FOR ADVANCED ESOPHAGEAL CANCER	2.0001
EST-2278	PHASE II CHEMOTHERAPY MASTER PROTOCOL AND MITOMYCIN-C VS CIS-PLATINUM FOR ADVANCED ESOPHAGEAL SQUAMOUS CELL CARCINOMA	2.0002
NCOG-3E81	PHASE II RADIOTHERAPY WITH HEAVY CHARGED PARTICLES FOR LOCALIZED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS	2.0003
RTOG-7709	HIGH DOSE VS LOW DOSE VS MIXED BEAM NEUTRON THERAPY FOR CARCINOMA OF THE ESOPHAGUS	2.0004
RTOG-7832	PHASE I-II MISONIDAZOLE THERAPY PRIOR TO RADIOTHERAPY FOR LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS	2.0005
SEG-GI-P35	PHASE I-II PILOT CHEMOTHERAPY WITH BLEOMYCIN/METHOTREXATE/CIS-PLATINUM PLUS RADIOTHERAPY FOR NON-GLANDULAR ESOPHAGEAL CARCINOMA	2.0006
SEG-GI-P39	PHASE II PILOT CHEMOTHERAPY WITH CIS-PLATINUM FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS	2.0007
SWOG-7806	PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR REFRACTORY EPIDERMOID CARCINOMA OF THE ESOPHAGUS	2.0008
GTSG-5377	PHASE II CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE VS MITOMYCIN-C FOR ADVANCED SQUAMOUS-CELL CARCINOMA OF THE ESOPHAGUS	2.0009
MDAR-338	PHASE II CHEMOTHERAPY WITH ABCX (ADR/BLEO/CACP PLUS RADIOTHERAPY) FOR SQUAMOUS CELL CARCINOMA OF THE CERVICAL ESOPHAGUS	2.0010
MSKCC-7961	COMBINATION CHEMOTHERAPY WITH CIS-PLATINUM/VINDESINE/BLEOMYCIN FOR METASTATIC OR RECURRENT SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS	2.0011
MI-ESO-1	BCG IMMUNOTHERAPY AND RADIOTHERAPY ALONE OR IN COMBINATION AFTER SURGERY IN DISSEMINATED ESOPHAGEAL CANCER	2.0012
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EORTC-40762	RADIOTHERAPY FOLLOWED BY SURGERY VS SURGERY ALONE FOR RESECTABLE SQUAMOUS-CELL CARCINOMA OF THE ESOPHAGUS	2.0015
EORTC-40763	CHEMOTHERAPY WITH METHOTREXATE PRECEDING RADIOTHERAPY VS RADIOTHERAPY ALONE FOR INOPERABLE CARCINOMA OF THE ESOPHAGUS	2.0016
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EST-PF-279 A PILOT STUDY OF COMBINATION CHEMOTHERAPY WITH 5-FU/ADR/CACP FOR ADVANCED GASTRIC CANCER 2.0021

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MI-CRC-113628D ADJUVANT IMMUNOTHERAPY WITH BCG IN COLORECTAL CARCINOMA 2.0107
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NCCTG-784852 ADJUVANT LEVAMISOLE IMMUNOTHERAPY WITH VS WITHOUT 5-FLUOROURACIL FOR SURGICALLY CURED COLORECTAL CARCINOMA 2.0111
NCCTG-794751 POSTOPERATIVE RADIOTHERAPY ALONE VS POSTOPERATIVE MECCNU/5-FU SEQUENTIAL CHEMOTHERAPY PLUS RADIOTHERAPY FOR RECTAL CARCINOMA 2.0112

SJCRH-GIC-1 PHASE III CHEMOTHERAPY WITH VCR/MECCNU/5-FU FOR CARCINOMA OF THE COLON IN CHILDREN 2.0113

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2F. GASTROINTESTINAL—GENERAL

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GUMO-11 PHASE II EVALUATION OF CACP IN PATIENTS WITH RESIDUAL, RECURRENT, OR METASTATIC GASTRIC OR PANCREATIC ADENOCARCINOMA 2.0122

MDAR-312 ADJUVANT CHEMOTHERAPY WITH 5-FU/ADR/MITO FOLLOWING CURATIVE RESECTION FOR ADENOCARCINOMA OF THE STOMACH OR ESOPHAGUS 2.0123

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MI-GI-2 IMMUNOTHERAPY WITH BCG IN CANCERS OF THE STOMACH, SMALL BOWEL, BILIARY TRACT, AND PANCREAS 2.0125

NC-GI-1 SELECTIVE HEPATIC DEARTERIALIZATION, INTRAPERITONEAL BCG AND CHEMOTHERAPY FOR EXTENSIVE INTRA-ABDOMINAL CANCER WITH LIVER METASTASES 2.0126

NCCTG-784851 PHASE III CHEMOTHERAPY WITH 5-FU VS 5-FU/ADR VS 5-FU/ADR/MITO FOR ADVANCED UPPER GASTROINTESTINAL ADENOCARCINOMA 2.0127

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RPMI-PPC-524 RADIOTHERAPY AND CHEMOTHERAPY WITH ADR FOR LOCALIZED, UNRESECTABLE CARCINOMA OF THE STOMACH, PANCREAS, AND BILIARY TREE 2.0129

CAN-CCI-GI-1 PHASE II ADJUVANT COMBINATION CHEMOTHERAPY WITH 5-FU/MECCNU PLUS BCG IMMUNOTHERAPY IN GASTROINTESTINAL CANCER 2.0130

CAN-UICC-7501 POST-SURGICAL ADJUVANT BCG IMMUNOTHERAPY AND 5-FU CHEMOTHERAPY FOR ADENOCARCINOMA OF THE STOMACH, PANCREAS, COLON OR RECTUM 2.0131

ITA-GI-1 DOUBLE-BLIND EVALUATION OF ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE PRE- AND POSTOPERATIVELY FOR GASTROINTESTINAL CANCER ... 2.0132

JAP-GI-1 IMMUNOCHEMOTHERAPY WITH LEVAMISOLE, MITO, AND FT-207 VS CHEMOTHERAPY WITH MITO AND FT-207 FOR GASTROINTESTINAL CANCER 2.0133

JAP-GI-2 IMMUNOTHERAPY WITH BCG, PSK, OK-432 WITH/WITHOUT CHEMOTHERAPY WITH FT ADJUVANT TO SURGERY FOR ADVANCED GASTROINTESTINAL CANCER 2.0134

SECTION 2

GASTROINTESTINAL TUMORS

2A. ESOPHAGUS

2.0001 PILOT STUDY OF CHEMOTHERAPY WITH MTX/BLM/METHYL-GAG/CIS-PLATINUM FOR ADVANCED ESOPHAGEAL CANCER

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PROTOCOL NUMBER(S) EST-PB-279

OBJECTIVES:

I. Determine tolerability (toxicity) of a combination of the four agents under study with respect to the oral and esophageal mucosae.

II. Gather preliminary data on the efficacy of combined methotrexate (MTX), bleomycin, (BLM), methyl-GAG (MeGAG), and cis-platinum (CACP) in advanced esophageal cancer.

PROTOCOL ENTRY CRITERIA: Patients with proven histologic diagnosis of squamous esophageal cancer, incurable by radiation or surgery, with measurable tumor. Previous palliative radiotheraphy, or chemotherapy with other than one or more of the four agents in this study, does not disqualify. Hydrated serum creatinine must be less than 1.5 mg/dl, creatinine clearance greater than 40 ml/min/sqm, WBC must be greater than 4000, platelet count greater than 100, 000/ml. No obstructive uropathy evident.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; Bleomycin, BLM, NSC-125066; Methyl-GAG, MeGAG, NSC-32946; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: SMA - 6 and 12; creatinine clearance.

END POINTS: Toxicity/morbidity of treatment.

CURRENT STATUS: None given.

DOSAGE SCHEDULE:

21-day cycle. MeGAG - 500 mg/sqm iv in 100 ml D5W over 30 min on days 1 and 15; MTX - 40 mg/sqm im on days 1 and 15; BLM - 10 U im on days 1, 8, and 15; CACP - 50 mg/sqm iv on day 4. CACP given 30 min after institution of iv infusion of D5 1/2 NS plus 10 mEq KCl/liter at rate of 1 liter per hour for 2 hours. 40 mg Furosemide iv at start of infusion, 12.5 g mannitol iv immediately before CACP. Maintenance: Repeat 21-day cycle. Discontinue Bleomycin after total cumulative dose of 400 U, continue other 3 drugs. A minimum of 6 weeks (2 full cycles) is given. Treatment is continued until progressive disease or prohibitive toxicity develops.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 50 mg vials; BLM - 15 IU ampules; CACP - 10 mg vials; MeGAG - 1 g vials.

DATE SUMMARIZED: 02/80

2.0002 PHASE II CHEMOTHERAPY MASTER PROTOCOL AND MITOMYCIN-C VS CIS-PLATINUM FOR ADVANCED ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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PROTOCOL NUMBER(S) EST-2278

OBJECTIVES:

I. Screen new agents and drug combinations for activity in patients with inoperable advanced, measurable esophageal squamous cell carcinoma.

II. Compare the efficacy of mitomycin-C and cis-platinum for this disease.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically confirmed, advanced inoperable squamous cell carcinoma of the esophagus. Patients must have a performance status better than 4, caloric intake should exceed 1500 calories per day and fluid intake over 1500 ml per day. Patients must have adequate bone marrow, hepatic and renal function. Prior chemotherapy should be completed more than 3 weeks prior to entry and radiotherapy to measurable lesions must have failed to halt progression.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Mitomycin-C, MITO, NSC-26980.

Arm II: Single-agent Chemotherapy. Cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Performance status: 0 or 1 vs. 2 or 3; prior chemotherapy; prior radiotherapy; participating institutions.

SPECIAL STUDY PARAMETERS: Liver, bone, brain scan; IVP; plus audiogram and creatinine clearance for Arm II patients.

END POINTS: Objective tumor response, response rate, duration of response, survival time.

CURRENT STATUS: 50 patients will be entered within 2 years.

DOSAGE SCHEDULE:

Arm I: MITO - 20 mg/sqm iv q 4 weeks for 2 courses, then q 6 weeks. Remove patients with progressive disease after 2 courses from study; continue all others until progression or unmanageable toxicity.

Arm II: CACP - 50 mg/sqm iv q 3 weeks with adequate hydration, furosemide and mannitol.

Remove patients with progressive disease after 2 courses from study; continue all others until progression or unmanageable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MITO - 5 mg vials; CACP - 1 mg vials.

DATE SUMMARIZED: 12/78

2.0003 PHASE II RADIOTHERAPY WITH HEAVY CHARGED PARTICLES FOR LOCALIZED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS

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PROTOCOL NUMBER(S) NCOG-3E81; RTOG-7909

OBJECTIVES:

I. Evaluate local and regional tumor control, response duration and the incidence of local relapse following heavy charged-particle therapy.

II. Evaluate survival including quality of survival and disease-free interval.

III. Evaluate normal tissue response and tolerance.

IV. Evaluate the technical aspects of treatment planning in an attempt to maximize the therapeutic ratio by minimizing the normal tissue volume to be irradiated.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven squamous cell carcinoma of the esophagus, AJC Stage I or II, with disease in regional, including supraclavicular or celiac, lymph nodes permitted. Patients must have a Karnofsky score of at least 50%, a life expectancy of least 6 months, must not have had significant radiotherapy to areas to be treated and no distant metastases.. Prior, but not concomitant, chemotherapy is acceptable.

PROTOCOL OUTLINE: Nonrandomized study.

Heavy Charged-Particle Radiotherapy. 934 MeV helium ion beam from 184-inch cyclotron at the Lawrence Berkeley Laboratory.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Esophagram, esophagoscopy, liver scan or biopsy, lung tomography, CAT scan, SMA-12 or SMA-6.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival time, survival rate, duration of response, relapse rate, quality of survival.

CURRENT STATUS: 30 to 60 patients will be entered.

DOSAGE SCHEDULE:

800 rad CoRE (Cobalt-60 rad equivalent dose) in 7 days given in 4 equal fractions for a total initial dose of 6000 rad CoRE given in 30 fractions over 7 1/2 weeks to the entire primary tumor and all involved regional lymph nodes. If tolerance is acceptable in the first 10 patients entered, escalate dose by 50%, then subsequently by 5% in groups of 10 patients each, if no unacceptable toxicity occurs. Follow up all patients q 2 months for 6 months, q 4 months for 18 months and q 6 months thereafter. Patients with progressive, recurrent and/or metastatic disease may receive Chemotherapy. Follow all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 05/79

2.0004 HIGH DOSE VS LOW DOSE VS MIXED BEAM NEUTRON THERAPY FOR CARCINOMA OF THE ESOPHAGUS

Brady, L., (215-574-3150) Radiation Therapy Oncology Group,
925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) RTOG-7709

OBJECTIVES:

I. Determine if local control of the primary is improved by fast neutron radiotherapy, compared to traditional treatment methods.

II. Determine the tolerance of surrounding normal tissue and complication rates.

III. Determine the incidence of distant metastases.

IV. Determine the survival rate.

V. Determine the quality of survival rate as reflected by the Karnofsky Performance Status.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with histologically confirmed, untreated, squamous cell carcinoma of the esophagus staged according to the TNM classification and with lesions no more than 15 cm in length. Patients must not have positive supraclavicular or celiac nodes, distant metastases or fistulas or sinus tract on esophagram.

PROTOCOL OUTLINE: Nonrandomized study. Sequential, eligible patients will be treated according to one of the protocol treatment regimens, selected prior to registration.

Regimen A: Neutron Radiotherapy in High Dosage Treatments.

Regimen B: Neutron Radiotherapy in Low Dosage Treatments.

Regimen C: Mixed-beam Radiotherapy.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: LFT, liver scan, esophagram, SMA-12.

END POINTS: Response/remission rate, survival rate, toxicity/morbidity of treatment, quality of survival, appearance of local recurrence or distant metastases.

CURRENT STATUS: 55 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Treat supraclavicular area and mediastinum followed by an additional boost to the primary tumor.

Regimen A: Neutron Radiotherapy - 6000 rads in 6 weeks, given in two 500-rad fractions per week.

Regimen B: Neutron Radiotherapy - 6000 rads in 6 weeks, given in four 250-rad fractions per week.

Regimen C: Mixed Beam Radiotherapy - 6000 rad equivalents given in 6 weeks in 2 neutron and 3 photon fractions per week at 200 rad/fraction.

Follow up all patients q 3 months for 2 years and q 6 months for the subsequent 3 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 08/78

2.0005 PHASE I-II MISONIDAZOLE THERAPY PRIOR TO RADIOTHERAPY FOR LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS

Brady, L., (215-574-3150) Radiation Therapy Oncology Group,
925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) RTOG-7832

OBJECTIVES:

I. Determine the tolerance of misonidazole in a larger group of patients with less advanced disease based on experience obtained in the Phase I Study in the RTOG.

II. Determine the tolerance of the unusual radiation fractionation scheme proposed in this protocol in terms of acute and late normal tissue reaction and damage.

III. Observe the relationship between dose of misonidazole in mg/m2, mg/kg, and the 4 to 6 hour blood level of misonidazole.

IV. Establish that the tumor clearance rate, disease-free interval, local tumor control rate and tumor relapse patterns are within the expected ranges for this type and stage of disease.

V. Lay the basis for a randomized Phase III study of misonidazole in squamous cell carcinoma of the esophagus.

PROTOCOL ENTRY CRITERIA: Patients aged 18 to 80 years with histologically proven, advanced and measurable squamous cell carcinoma of the esophagus, Stages II or III without distant metastases, tracheobronchial fistula, mediastinitis, malignant pleural effusions or complete obstruction preventing therapy. Patients may have recurrent disease following surgery, but must not have had radiotherapy. They may have squamous cell carcinoma of any histological grade. Patients must have a life expectancy of at least 4 months, a Karnofsky performance status of at least 50, adequate hemotologic, renal and hepatic functions and acceptable neurologic and metabolic status. They may not have had prior radiotherapy, must have been off any prior chemotherapy for 2 weeks before study entry and must have recovered from any toxicities from such therapy. They may not be taking more than 1 g/day of Vitamin C.

PROTOCOL OUTLINE: Nonrandomized study.

Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037; plus megavoltage radiation, Cobalt-60 to 25 MeV.

STRATIFICATION BY: Disease stage, histologic grade, Karnofsky status, prior surgery.

SPECIAL STUDY PARAMETERS: Liver scan, upper GI series, esophagus, liver scan and lung tomogram if indicated.

END POINTS: Toxicity/morbidity of treatment, objective tumor response, disease-free interval, recurrence rate, response/remission rate, response duration.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

MNI - 1.25 g/sqm (maximum cumulative dose 15 g/sqm) po given 2 or 3 times a week depending on Radiotherapy schedule 4 to 6 hours prior to each Radiotherapy treatment for a total of 12 doses. Monitor 4 to 6 hour MNI mean plasma levels.

Radiotherapy - 4400 to 4800 rad given to the esophagus from the thoracic inlet to the gastric cardia in no more than 5 weeks in 12 fractions of 400 rad each with a field reduction after 3200 rad.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Misonidazole - 100 and 500 mg capsules.

DATE SUMMARIZED: 05/79

2.0006 PHASE I-II PILOT CHEMOTHERAPY WITH BLEOMYCIN/METHOTREXATE/CIS-PLATINUM PLUS RADIOTHERAPY FOR NON-GLANDULAR ESOPHAGEAL CARCINOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America

PROTOCOL NUMBER(S) SEG-GI-P35

OBJECTIVES:

I. Determine toxicity of combination chemotherapy (bleomycin, methotrexate, cis-platinum) with radical radiotherapy for carcinoma of the esophagus.

II. Test the effectiveness of chemotherapy preceding radiotherapy in terms of: primary tumor control, reduction of distant metastases, and increase in surgical resectability.

III. Proceed ultimately with a randomized study to compare the stated chemotherapy-radiotherapy regime versus radiotherapy only in non-glandular carcinoma of the esophagus.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with a measurable lesion of diagnostically confirmed non-glandular carcinoma of the esophagus. Patients must have adequate pulmonary function and a baseline creatinine clearance of at least 60 ml/min.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy followed by Radiotherapy. Bleomycin, BLEO, NSC-125066; Methotrexate, MTX, NSC-740; cis-Platinum, CACP, NSC-119875; plus Radiotherapy with photon energy of 1 MeV or higher.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Esophagogram, liver scan, audiometry, pulmonary function tests, surgical staging desirable.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, reduction of metastases, resectability, objective tumor response.

CURRENT STATUS: 14 to 29 patients will be entered.

DOSAGE SCHEDULE:

BLEO - 15 units/day iv infusion for 48 hours on days 0 and 1; MTX - 25 mg/sqm (maximum dose 50 mg) im on day 4; CACP - 60 mg/sqm iv with adequate hydration on day 7. Repeat course once beginning on day 14 for a total of 2 courses. When significant toxicity has abated, begin Radiotherapy - 5000 rad in 20 fractions of 250 rad over a period of 4 weeks to the primary tumor, its direct extensions and nearby involved lymph nodes. Evaluate all patients 8 weeks after the end of Radiotherapy. Further therapy is at the investigator's option. Follow up all patients q 6 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 unit vials; MTX - 5 and 50 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 07/79

2.0007 PHASE II PILOT CHEMOTHERAPY WITH CIS-PLATINUM FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America

PROTOCOL NUMBER(S) SEG-GI-P39

OBJECTIVES:

I. Evaluate the therapeutic effectiveness and toxicity of cis-platinum in the treatment of advanced squamous cell carcinoma of the esophagus.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed advanced squamous cell carcinoma of the esophagus who are not eligible for surgical resection. Patients must have a measurable lesion, a Karnofsky performance status of at least 50% and an estimated life expectancy greater than 6 weeks. There must have been no prior major surgery or other therapy within 30 days of entry. Creatinine must be above 2 mg/100 ml and there must be adequate hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Audiogram, CEA, scans as needed, esophagogram, liver measurements, measurements of metastatic lesions.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 14 to 25 patients will be entered.

DOSAGE SCHEDULE:

CACP - 90 mg/sqm iv q 3 weeks for a minimum of 2 courses with prior and subsequent hydration and mannitol diuresis. Consider patients with rapid disease progression after 1 course to be treatment failures. Remissions should be maintained for at least one month following documentation of initial response. Continue therapy for patients who are continuing to respond after 2 courses until disease progression or unacceptable toxicity. Follow up patients q 3 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 07/79

2.0008 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR REFRACTORY EPIDERMOID CARCINOMA OF THE ESOPHAGUS

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PROTOCOL NUMBER(S) SWOG-7806

OBJECTIVES:

I. Determine the response rate and survival with some degree of precision, utilizing cis-platinum (CACP) in the treatment of squamous-cell carcinoma of the esophagus.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-confirmed epidermoid carcinoma of the esophagus, excluding adenocarcinoma. Patients must have an absolute granulocyte count of at least 2000, a platelet count of at least 150,000, two adequately functioning kidneys and an unobstructed urinary tract.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Measurable vs. nonmeasurable disease; performance status: 0-1 vs. 2 or higher; participating institutions.

SPECIAL STUDY PARAMETERS: Esophagram, prostate exam (males), blood counts, renal and liver function tests, uric acid, albumin, total protein, IVP, audiogram.

END POINTS: Response/remission rate, objective tumor response, survival, relapse rate.

CURRENT STATUS: About 45 patients will be entered in 17-25 months.

DOSAGE SCHEDULE:

CACP - 50 mg/sqm iv given over an interval of 1 to 4 hours on days 1 and 8 q 28 days. Repeat therapy at this dosage if BUN is no greater than 20 mg%, creatinine no greater than 1.4 mg%, creatinine clearance at least 75 cc/mm, wbc and platelet counts at least 4000 and 150,000, respectively. Increase subsequent doses by 20% and continue at level of tolerable toxicity as long as there is evidence of tumor regression or disease stability. Follow all patients until clinical relapse and for life. Follow tumor measurements in patients with measurable disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00110279

2.0009 PHASE II CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE VS MITOMYCIN-C FOR ADVANCED SQUAMOUS-CELL CARCINOMA OF THE ESOPHAGUS

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PROTOCOL NUMBER(S) GTSG-5377

OBJECTIVES:

I. Determine whether cyclophosphamide or mitomycin-C can improve palliation or survival in patients with advanced, recurrent, or unresectable squamous-cell carcinoma of the esophagus.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven squamous-cell carcinoma of the esophagus, inoperable, proven residual or with metastases, who have failed to respond to prior surgery or radiation therapy. Patients must have a performance status better than 4, adequate nutritional status and wbc and platelet values. Patients must not have active renal disease, previous treatment with mitomycin-C or any alkylating agent.

PROTOCOL OUTLINE: Randomized study. Enter patients with active renal disease to Arm I only.

Arm I: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm II: Single-agent Chemotherapy. Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Measurable disease, prior radiation therapy, performance status, renal disease status, participating institutions.

SPECIAL STUDY PARAMETERS: Liver scan, immunological and skin test responses.

END POINTS: Objective tumor response, duration of response, response/remission rate, survival, time to regression.

CURRENT STATUS: 80 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: CTX - 1000 mg/sqm iv on day 1 q 3 weeks. Repeat to clinical toxicity or death.

Arm II: MITO - 20 mg/sqm iv on day 1 q 6 weeks. Repeat to clinical toxicity or progression.

Cross over patients with active progression after six weeks to alternate Arm if still eligible, otherwise remove from study. Follow patients till death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; MITO - 5 mg vials.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00061278

2.0010 PHASE II CHEMOTHERAPY WITH ABCX (ADR/BLEO/CACP PLUS RADIOTHERAPY) FOR SQUAMOUS CELL CARCINOMA OF THE CERVICAL ESOPHAGUS

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PROTOCOL NUMBER(S) MDAR-338; MDA-GE-794

OBJECTIVES:

I. Determine whether ABCX: the combination of adriamycin (ADR), bleomycin (BLEO) and cis-platinum (CACP) with radiation therapy achieves not only temporary local control of the tumor but also possible control of subclinical metastatic disease.

II. Determine local control rates and survival with this regimen.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with histologically confirmed squamous cell carcinoma of the cervical and upper thoracic esophagus, with nonresectable local or local plus widespread subclinical metastatic disease. Patients must not have had prior radiation, chemotherapy or immunotherapy and must have an expected survival time of at least 8 weeks and an adequate hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Induction:

3-Drug Combination Chemotherapy plus Radiotherapy and Nutritional Therapy. ABCX: Adriamycin, ADR, NSC-123127; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875; plus Radiotherapy; plus Intravenous Hyperalimentation (IVH).

Maintenance:

2-Drug Combination Chemotherapy. ADR, CACP.

STRATIFICATION: Primary tumor site: cervical vs. upper thoracic; metastasis: absent vs. present.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Temporary local tumor control, control of subclinical metastatic disease, response/remission rate, survival time, survival rate, objective tumor response.

CURRENT STATUS: 20 patients will be entered in 6 months.

DOSAGE SCHEDULE:

Induction:

ABCX: Radiotherapy - 2500 rads weekly for 2 weeks; ADR-25 mg/sqm (total cumulative dose 350 mg/sqm) iv on days 1 and 2; BLEO - 15 mg (total cumulative dose 120 mg) by 24 hour continuous iv on days 1 through 4; CACP - 25 mg/sqm given iv q 4 hours on days 3, 4 and 5. Give intravenous hyperalimentation (IVH) for 15 to 30 days if indicated. Repeat ABCX course on day 30 if there is no evidence of significant mucositis.

Maintenance:

ADR - 25 mg/sqm iv on days 1 and 2; CACP - 25 mg/sqm given iv q 4 hours on days 3, 4 and 5.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/79

2.0011 COMBINATION CHEMOTHERAPY WITH CIS-PLATINUM/VINDESINE/BLEOMYCIN FOR METASTATIC OR RECURRENT SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS

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PROTOCOL NUMBER(S) MSKCC-7961

OBJECTIVES:

I. Evaluate the effect of cis-platinum (CACP)/vindesine (DAVA)/bleomycin (BLEO) on the response rate and response duration of patients with metastatic squamous cell carcinoma of the esophagus.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically or cytologically confirmed metastatic or recurrent squamous cell carcinoma of the esophagus. Patients must have Class I or II (N.Y. Heart Association) cardiac status, and adequate renal and auditory function. Patients must not have had prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Vindesine, DAVA, NSC-245467; Bleomycin, BLEO, NSC-125066.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: SMA-12, pulmonary function, barium esophagram, liver scan.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, survival, duration of response.

CURRENT STATUS: About 25 patients will be entered in 12 to 18 months.

DOSAGE SCHEDULE:

CACP - 120 mg/sqm (route not given) on days 1 and 29, then q 6 weeks; DAVA - 3 mg/sqm (route not given) on days 1, 8, 15, 23, 29, 35 and 43, then q 2 weeks; BLEO - 10 U/sqm iv push loading dose; then 10 U/sqm iv infusion on days 3 through 6 and 29 through 32. Follow all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

2.0012 BCG IMMUNOTHERAPY AND RADIOTHERAPY ALONE OR IN COMBINATION AFTER SURGERY IN DISSEMINATED ESOPHAGEAL CANCER

Kerry, R. L., (313-973-2800) St. Joseph's Mercy Hospital, P.O. Box 995, Ann Arbor, Michigan, 48106, United States of America

PROTOCOL NUMBER(S) MI-ESO-1

OBJECTIVES:

I. Determine whether immunotherapy with BCG will improve the remission and survival time of patients with disseminated esophageal cancer who may have already undergone surgery or radiotherapy or both.

PROTOCOL ENTRY CRITERIA: Patients with disseminated or advanced esophageal cancer.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: Radiotherapy.

Arm III: Radiotherapy plus Immunotherapy. BCG.

Arm IV: No further treatment.

STRATIFICATION BY: Participating institutions; staging by the American Joint Committee.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 50 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BCG vaccine - one ampule (2-8 x 10 to the eighth colony forming units) po. BCG will be given before surgery and within 4 weeks after surgery as a course of adjuvant Immunotherapy given by the multiple-puncture tine technique in both axillae and both groin areas for 3 weeks. Oral administration will start at the same time and be given for 12 weeks, then every other week for 2 years. Initial dosage of one ampule of diluted BCG po may gradually be reduced to 1/10 ampule over the 12-week period. If presurgical treatment with BCG is used, treatment will be started with the oral and the multiple-puncture tine technique vaccination.

Arm II: Radiotherapy - dosage not specified.

Arm III: Radiotherapy as in Arm II; BCG as in Arm I.

Arm IV: No further treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - ampules containing 2-8 x 10 to the eighth CFU.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

2.0013 ADJUVANT IMMUNOTHERAPY WITH BCG AND RADIOTHERAPY ALONE AND COMBINATION FOR ESOPHAGEAL CARCINOMA

Kerry, R. L., (313-973-2800) St. Joseph's Mercy Hospital, P.O. Box 995, Ann Arbor, Michigan, 48106, United States of America

PROTOCOL NUMBER(S) MI-ESO-2

OBJECTIVES:

I. Compare adjuvant immunotherapy using BCG-Tice (BCG) with radiation therapy and the combination of the two with respect to the cure rate of carcinoma of the esophagus potentially cured by surgery.

PROTOCOL ENTRY CRITERIA: All patients who have had a primary esophageal carcinoma excised and have no known metastases.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: Radiotherapy.

Arm III: Radiotherapy plus Immunotherapy. BCG as in Arm I; plus Radiotherapy as in Arm II.

Arm IV: No further treatment.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Response/remission rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BCG - id by multiple-puncture tine technique in both axillae, parasternal, and supraclavicular areas before and within 4 weeks after surgery for 3 weeks, followed by BCG - 1 ampule po for 12 weeks, then every other week for 2 years. Dosage will be reduced to 1/10 ampule over the 12-week period.

Arm II: Radiotherapy. Details not given.

Arm III: Immunotherapy as in Arm I plus Radiotherapy as in Arm II.

Arm IV: No treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCG - ampules containing 2-8 x 10 to the eighth CFU.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

2.0014 PHASE II HIGH VS LOW DOSE MTX VS CACP PLUS SURGERY AND/OR RADIATION WITH OR WITHOUT MER FOR EPIDERMOID CARCINOMA OF THE ESOPHAGUS

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PROTOCOL NUMBER(S) ARG-HN-7704

OBJECTIVES:

I: Evaluate the use of early high dose chemotherapy to reduce tumor mass before radical treatment with radiation and surgery.

II: Use cis-Platinum (CACP) and Methotrexate (MTX) in high and low dose schedules.

III: Evaluate in a Phase II study these drugs in early disease and assess the impact of early chemotherapy upon remission rates and survival.

IV: Evaluate maintenance immunotherapy with MER following definitive radiotherapy or surgery.

PROTOCOL ENTRY CRITERIA: Patients with previously untreated, histopathologically diagnosed epidermoid carcinoma of the esophagus eligible for conventional radical treatment. Patients must have adequate bone marrow, renal and hepatic function and must be staged by the TNM system.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I: 2-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

Arm II: Single-agent Chemotherapy. MTX.

Arm III: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Following definitive therapy with radiation, with or without surgery as appropriate, evaluate presence of residual disease, and rerandomize patients free of apparent disease to Arm IV or V.

Maintenance:

Arm IV: Single-agent Immunotherapy. MER-BCG, MER, NSC-143769.

Arm V: No treatment.

STRATIFICATION BY: Participating institutions; for second randomization: definitive radiation vs. radiotherapy plus surgical resection.

SPECIAL STUDY PARAMETERS: Esophagoscopy, liver and lung scans, skin test for recall antigens, immunological studies, biopsy review.

END POINTS: Response/remission rate, survival rate, relapse free interval, relapse rate, relapse pattern.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: MTX - 1.5 g/sqm iv on day 1 and 2.5 g/sqm on day 8 with hydration; CF - 12 mg/sqm iv q 6 hours for 12 doses starting 2 hours after MTX. CF may be given po for the last 8 doses.

Arm II: MTX - 50 mg/sqm iv on day 1 and 5 mg/sqm on day 8.

Arm III: CACP - 50 mg/sqm iv on days 1 and 2 with hydration and diuresis.

Evaluate all patients in Arms I, II and III on day 15 and enter to definitive therapy on day 18. Enter patients with resectable disease to Surgery plus Radiotherapy, patients with nonresectable lesions above the aortic arch to Radiotherapy alone.

Radiotherapy: Enter all patients. 5500-6000 rad in 6 weeks for patients not considered for Surgery, 2000 rad in 5 days for others prior to surgical resection.

Surgery: Resection of primary tumor 2 days following Radiotherapy.

Maintenance: Randomized study for patients free of apparent disease to Arm IV or V.

Arm IV: MER - 1 mg total dose sc in 5 sites on the back, then lower dose to 0.5 mg total dose given once a month to 5 sites for 18 months.

Arm V: No Maintenance therapy.

Remove patients with progressive disease from study. Follow all patients for survival.

Dosage modifications for toxicity for MTX are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/79

PATIENT ACCRUAL: 00041078

2.0015 RADIOTHERAPY FOLLOWED BY SURGERY VS SURGERY ALONE FOR RESECTABLE SQUAMOUS-CELL CARCINOMA OF THE ESOPHAGUS

Gignoux, M., European Org. for Research on Treatment of Cancer, Gastrointestinal Tract Cooperative Group, Centre Regional Francois Baclesse, Route de Lion sur Mer, 14021 Caen Cedex, France

PROTOCOL NUMBER(S) EORTC-40762; UICC-75032

OBJECTIVES:

I. Compare treatment with presurgical radiotherapy vs. surgery alone for patients with operable epithelioma of the thoracic esophagus without distant metastases.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with curatively resectable squamous-cell carcinoma localized to the upper third or the upper part of the middle third portion of the esophagus. Patients must have no evidence of metastases (TX operable N0-NX-M0) and must be eligible for major thoracic surgery.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. High-energy or telecobalt followed by Surgery.

Arm II: Surgery.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Fiberoptic esophagoscopy and biopsy, CEA, liver scan.

END POINTS: Response rate, toxicity/morbidity of treatment, survival rate, duration of survival, quality of survival, surgical mortality rate, relapse rate, rate of appearance of metastases, rate of surgical complications.

CURRENT STATUS: 52 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

Arm I: 3350 rads given in 10 fractions over a period of 12 days to the tumor. Maintain patients on a high-calorie diet. Rest 8 days. Perform surgery for the removal of the tumor, resection of the lower part of the esophagus and reestablishment of the continuity of the digestive tract. Follow up patients q month for 3 months; q 3 months till the end of the second year and q 6 months thereafter.

Arm II: Surgery, as in Arm I. Perform simulated 'placebo' radiotherapy and/or delay surgery 16 to 20 days during which give patients the same high-calorie diet and medical treatment administered to patients in Arm I.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 01/77

2.0016 CHEMOTHERAPY WITH METHOTREXATE PRECEDING RADIOTHERAPY VS RADIOTHERAPY ALONE FOR INOPERABLE CARCINOMA OF THE ESOPHAGUS

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PROTOCOL NUMBER(S) EORTC-40763; UICC-77022

OBJECTIVES:

I. Compare methotrexate chemotherapy prior to radiotherapy with radiotherapy alone for inoperable cancer of the esophagus without metastases.

PROTOCOL ENTRY CRITERIA: Previously untreated patients less than 75 years old with inoperable squamous-cell carcinoma of the esophagus localized between 15 and 45 cm from the dental arch and without detectable nodal or visceral metastases; classification: TX inoperable N0-NX-M0. Patients must have adequate hematological and nutritional status and must not have lost more than 25% of their usual weight.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. High-energy photons or, if not available, telecobalt.

Arm II: Single-agent Chemotherapy plus Radiotherapy. Methotrexate, MTX, NSC-740. Radiotherapy as in Arm I.

STRATIFICATION BY: Participating institutions, tumor site.

SPECIAL STUDY PARAMETERS: Fiberoptic esophagoscopy and biopsy, CEA, liver scan.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, quality of survival, objective tumor response, quality of survival rate and time to appearance of local recurrences and distant metastases.

CURRENT STATUS: 152 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Arm I: A. Lesions localized in the upper third of the esophagus. 4050 rads given in 18 fractions to the tumor and bilaterally to the area of the supraclavicular nodes, plus 1575 rads given in 7 fractions to the tumor lesion alone. B. Lesions localized in the middle and lower third of the esophagus. 4050 rads given in 18 fractions to the tumor and to the area of the celiac nodes, plus 1575 rads given in 7 fractions to the tumor lesion alone.

Arm II: MTX - 2 mg/10 kg/day sc given in 4 divided doses for 4 days. Begin radiotherapy as in Arm I, 8 days at the earliest after completion of chemotherapy or when the hematological status permits.

Follow up all patients q 2 months in the first year, q 3 months in the second year and q 6 months thereafter.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/77

2.0017 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED ESOPHAGEAL CARCINOMA

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PROTOCOL NUMBER(S) URU-GI-7903; BCRP-7927

OBJECTIVES:

I. Determine the therapeutic efficacy of methyl-GAG in the treatment of advanced esophageal carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven, nonresectable squamous carcinoma of the esophagus; there must be residual, recurrent, or metastatic carcinoma, and measurable disease. Patients must have an expected survival greater than 8 weeks and adequate nutritional intake of at least 1500 calories per day and be ambulatory more than 50 percent of the time. Patients must not have a tracheosophageal or esophagobronchial fistula, a history of a previous second primary malignant neoplasm other than curatively resected basal cell carcinoma of the skin or surgically cured carcinoma in situ of the cervix, or prior treatment with methyl-GAG. Patients must have no chemotherapy or radiotherapy for 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic and renal function tests, partial thromboplastin times, prothrombin time, fibrinogen, CXR.

END POINTS: Response/remission rate, objective tumor response.

CURRENT STATUS: 10-20 patients will be entered initially; if there is evidence of clinical response, an additional 10-20 will be entered.

DOSAGE SCHEDULE:

MeGAG - 600 mg/sqm iv 60-minute infusion q week for 4 weeks. If no toxicity is observed, dose is increased by 100 mg/sqm. After 3 courses, patients with progressive disease or life-threatening toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeGAG - 1.0 g vials.

DATE SUMMARIZED: 10/80

2B. STOMACH

2.0018 PHASE III INDUCTION WITH 5-FU/ADR/MITO VS MITO/ADR PLUS MITO/5-FU MAINTENANCE FOR ADVANCED GASTRIC CANCER

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America

PROTOCOL NUMBER(S) CLB-7981

OBJECTIVES:

I. Compare effect of induction with 5-fluorouracil (5-FU)/adriamycin (ADR)/mitomycin C (MITO) vs. intensive induction with MITO/ADR followed by common maintenance with MITO/5-FU for locally advanced or metastatic gastric adenocarcinoma.

II. Compare psychological distress of above patients with that of metastatic pancreatic cancer patients on protocol CLB-7982.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with histologically confirmed gastric adenocarcinoma which is surgically incurable and locally advanced (measurable or nonmeasurable) or metastatic (measurable). Patients must have an ECOG performance rating of at least 3, normal liver and adequate cardiac, kidney and hematologic function and must not have had prior radiation or chemotherapy.

PROTOCOL OUTLINE: Randomized study for induction only.

Induction:

Arm I: 3-Drug Combination Chemotherapy. FAM: 5-Fluorouracil, 5-FU, NSC-091893; Adriamycin, ADR, NSC-123127; Mitomycin C, MITO, NSC-026980.

Arm II: 2-Drug Combination Chemotherapy. MA: MITO; ADR.

Maintenance: Enter all patients who have shown at least partial response. 2-Drug Combination Chemotherapy. MF: MITO; 5-FU.

STRATIFICATION: Participating institutions; measurability; performance status: 0 or 1 vs. 2 or 3; tumor site: intra-abdominal vs. extra-abdominal; localized vs. metastatic.

SPECIAL STUDY PARAMETERS: Tumor measurement; kidney, liver, hematologic and bone function; liver and brain scan; bone x-ray; ultrasound or CAT scan; bone marrow aspirate; psychosocial assessment.

END POINTS: Response/remission rate, duration of response, time to progression, recurrence rate, objective tumor response, survival rate, survival time, toxicity/morbidity of treatment, rate of psychologic distress.

CURRENT STATUS: 170 patients will be entered in 27 months.

DOSAGE SCHEDULE:

Induction:

Arm I: FAM: 5-FU - 600 mg/sqm iv on days 1, 8, 29 and 36; ADR - 30 mg/sqm (maximum cumulative dose 480 mg/sqm) iv on days 1 and 29; MITO - 10 mg/sqm iv on day 1. Repeat course q 8 weeks for a total of 8 courses.

Arm II: MA: MITO - 10 mg/sqm iv on day 1; ADR - 50 mg/sqm (maximum cumulative dose 500 mg/sqm) iv on days 1 and 22. Repeat course q 6 weeks for a total of 5 courses.

Maintenance: Enter all patients who have achieved at least a partial response after the maximum dose of ADR has been reached. Start therapy 3 weeks after total ADR dose has been reached or the last dose of induction therapy (day 449 for Arm I; day 211 for Arm II) has been given. MF: MITO - 10 mg/sqm iv on day 1; 5-FU - 600 mg/sqm iv on days 1, 8, 29, 36. Repeat course q 56 days until patient develops progressive disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MITO - 5 and 20 mg vials; ADR - 10 and 50 mg vials; 5-FU - 10 ml ampules.

DATE SUMMARIZED: 09/79

2.0019 SURGICAL ADJUVANT SYSTEMIC CHEMOTHERAPY WITH FAM (5-FU/ADR/MITO) VS SURGERY ALONE FOR T2-4, N1-2 GASTRIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) CLB-7983

OBJECTIVES:

I. Determine whether six 2-month cycles of 5-fluorouracil/adriamycin/mitomycin-c following potentially curative surgery for adenocarcinoma of the stomach produces a longer disease-free survival than resection alone.

II. Determine tolerance to the chemotherapeutic regimen.

III. Evaluate the effect of the chemotherapy on patterns of recurrence.

IV. Evaluate whether this therapy is effective in any sub-groups of patients with gastric adenocarcinoma.

V. Compare survival of patients receiving adjuvant chemotherapy with that of patients observed without adjuvant treatment but receiving chemotherapy at the time of recurrent or metastatic disease.

VI. Observe systematically the emotional response of patients with early gastric cancer treated or not treated with adjuvant chemotherapy, with particular reference to depression.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven adenocarcinoma of the stomach or of the esophago-gastric junction treated by potentially curative surgery. The tumor must be staged at T2-4 and the nodal status must be negative or N1-2. Hematologic reserves and renal and hepatic function must be adequate. Patients must be entered into the protocol no more than 6 weeks after surgery. Patients must not have a history of significant heart failure and may not be over 70 years old.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery. Potentially curative surgery followed by observation.

Arm II: Surgery plus 3-Drug Combination Chemotherapy. Potentially curative surgery plus FAM: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Participating institutions, pathologic staging, surgical procedure, histological diagnosis.

SPECIAL STUDY PARAMETERS: Hematologic parameters, hepatic and renal function tests, CEA, liver scan, hepatic ultrasound, hepatic computerized tomography, chest x-ray, UGI, systolic ejection.

END POINTS: Disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: 176 patients will be required for the study and will be entered over a 3-year period.

DOSAGE SCHEDULE:

Arm I: Potentially curative surgery followed by observation. If recurrence occurs, patient will be removed from the protocol and placed on chemotherapy.

Arm II: Surgery followed by six 2-month cycles of FAM: 5-FU - 600 mg/sqm iv on days 1, 8, 29, and 36 of each cycle; MITO - 10 mg/sqm iv on day 1 of each cycle; ADR - 30 mg/sqm on days 1 and 29 of each cycle, total dose not to exceed 360 mg/sqm. Follow patients at 3-month intervals for 24 months, then at least q 6 months

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; ADR - 10 and 50 mg vials; MITO - 5 and 20 mg vials.

DATE SUMMARIZED: 06/80

2.0020 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR RECURRENT OR METASTATIC GASTRIC ADENOCARCINOMA

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Group, 905 University Ave., Suite 415, Madison, Wisconsin,
53715, United States of America
PROTOCOL NUMBER(S) EST-PE-279

OBJECTIVES:

I. Determine the activity of cis-platinum in patients with advanced gastric cancer who have failed standard chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed primary gastric adenocarcinoma beyond hope of surgical cure. The disease must be residual, recurrent, or metastatic and measurable; patients must have failed prior chemotherapy with either a single agent or a combination of drugs. Gastric lesions visualized by contrast radiography or of a size that can be only estimated are not considered measurable lesions. Carcinoembryonic or alpha-fetoprotein elevations do not constitute measurable disease. Hepatomegaly will be considered a measurable lesion if the liver has proven metastases or is palpable at least 5 cm below the xiphoid process. Measurable pulmonary lesions also constitute measurable disease. The performance status must be 0 through 3; 4 is excluded.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: SMA-6 and 12, audiogram.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

CACP - 75 mg/sqm iv infusion over 2 hours on days 1, 8, 15 and q 21 days thereafter, given with hydration with mannitol and furosemide. CR and PR patients continue until progression. Patients not achieving at least PR by day 78 will be taken off study. All patients will be followed until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 10/80

2.0021 A PILOT STUDY OF COMBINATION CHEMOTHERAPY WITH 5-FU/ADR/CACP FOR ADVANCED GASTRIC CANCER

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Group, 905 University Ave., Suite 415, Madison, Wisconsin,
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PROTOCOL NUMBER(S) EST-PF-279

OBJECTIVES:

I. Define a tolerable dose and schedule of a combination of 5-fluorouracil, adriamycin, and cis-platinum in the chemotherapy of advanced gastric cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented residual, recurrent, or metastatic adenocarcinoma of the stomach that is not amenable to curative surgical excision. Patients must be at least 3 weeks post major surgery, 2 weeks post explorative surgery, and 4 weeks post radiotherapy. Patients may not have had prior chemotherapy, must have a performance status of 0-3, and must not have any active infectious process. Hematological parameters must be adequate and there must be no azotemia or impaired liver function. Patients must not have had active heart disease within the previous 3 months.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurement, hematological parameters, liver and kidney function tests, chest x-ray, and audiogram.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: The estimated accrual is 10-15 patients.

DOSAGE SCHEDULE:

5-FU - 600 mg/sqm iv q 3 weeks; CACP - 50 mg/sqm iv infusion with concurrent furosemide-mannitol diureses, q 3 weeks; ADR - 50 mg/sqm iv q 3 weeks. Continue until the onset of prohibitive toxicity or progression of disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; ADR - 10 and 50 mg vials; 5-FU - 500 mg vials.

DATE SUMMARIZED: 07/80

2.0022 PHASE II/III CHEMOTHERAPY WITH COMBINATIONS OF MECCNU, MITO, ADR AND 5-FU FOR ADVANCED MEASURABLE GASTRIC CANCER

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Group, 905 University Ave., Suite 415, Madison, Wisconsin,
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PROTOCOL NUMBER(S) EST-2277

OBJECTIVES:

I. Evaluate the efficacy of combination chemotherapy with methyl CCNU (MeCCNU) and 5-fluorouracil (5-FU) vs. MeCCNU, 5-FU, and adriamycin (ADR) vs. mitomycin C (MITO) and ADR vs. MITO, ADR and 5-FU in the treatment of advanced measurable gastric cancer.

II. Evaluate the toxic 7-week regimens of MeCCNU/5-FU to determine whether an increased risk of toxicity is necessary to attain response rates similar to those in EST-1272 and whether the results seen in EST-1272 are reproducible.

III. Test the possibility that a combination of ADR and MITO might be as effective as 5-FU/MeCCNU. Patients previously treated with 5-FU and MeCCNU are eligible for this therapy.

IV. Compare the regimen of 5-FU, ADR and MITO giving a 50% objective response rate at Georgetown University Hospital to the MeCCNU plus 5-FU 7-week program.

V. Evaluate combination chemotherapy with 5-FU, ADR and MeCCNU which has also been demonstrated to be effective but with unacceptable toxicity. Increase the frequency of administration of MeCCNU without reducing the total dose to reduce toxicity. Compare these regimens in terms of response of toxicity to the 5-FU plus MeCCNU regimen.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven measurable disease of incurable residual recurrent or metastatic primary gastric adenocarcinoma who have had at least 3 weeks of recovery from major surgery, 2 weeks from minor surgery and 4 weeks from prior radiotherapy or chemotherapy. Patients must have adequate hematological, renal and hepatic functions, a performance status of less than 4 and should have no active heart disease.

PROTOCOL OUTLINE: Randomized study, except for patients with prior 5-FU or nitrosourea therapy. Enter these patients to Arm III only, and do not cross over nonresponders.

Arm I: 2-Drug Combination Chemotherapy. Methyl CCNU, MeCCNU, NSC-95441; 5-Fluorouracil, 5-FU, NSC-19893. Cross over nonresponders to Arm III.

Arm II: 3-Drug Combination Chemotherapy. MeCCNU; 5-FU; Adriamycin, ADR, NSC-123127.

Arm III: 2-Drug Combination Chemotherapy. Mitomycin C, MITO, NSC-26980; ADR. Cross over nonresponders to Arm I.

Arm IV: 3-Drug Combination Chemotherapy. MITO; ADR; 5-FU.

STRATIFICATION BY: Prior chemotherapy with 5-FU or nitrosourea; initial ECOG performance status; primary resection, time after initial histological diagnosis.

SPECIAL STUDY PARAMETERS. Liver function tests, renal function tests, prothrombin time.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: About 100 patients will be entered in 2-3 years.

DOSAGE SCHEDULE:

Arm I: MeCCNU - 175 mg/sqm po on day 1; 5-FU - 300 mg/sqm iv on days 1-5. Repeat course q 7 weeks. Cross over patients with disease progression or relapse to Arm III.

Arm II: MeCCNU - 60 mg/sqm po on days 1 and 22; 5-FU - 325 mg/sqm iv on days 1 through 5, 450 mg/sqm iv on day 22; ADR - 40 mg/sqm (maximum cumulative dose 540 mg/sqm) iv on days 1 and 22. Repeat course q 6 weeks.

Arm III: MITO - 12 mg/sqm iv on day 1; ADR - 36 mg/sqm iv on day 1 and 22. Repeat course q 6 weeks. Cross over patients with disease progression or relapse to Arm I. Remove nonresponders with prior 5-FU or nitrosourea therapy from study.

Arm IV: MITO - 10 mg/sqm iv on day 1; ADR - 30 mg/sqm iv on day 1 and 29; 5-FU - 600 mg/sqm iv on day 1, 8, 29 and 36. Repeat course q 6 weeks.

Remove patients with disease progression who are not eligible for cross-over therapy from study after one complete course of therapy. Patients with regression or stable disease remain on study until disease progression or general deterioration.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeCCNU - 10, 20, and 100 mg capsules; ADR - 10 and 50 mg vials; 5-FU - 500 mg vials; MITO - 5 mg vials.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00431178

2.0023 PHASE III CHEMOTHERAPY WITH ADR/5-FU VS BCNU/ADR/FTORAFUR VS MITO/ADR/FTORAFUR FOR DISSEMINATED GASTRIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) NCOG-3S62

OBJECTIVES:

I. In this U.S.-Japan Joint Protocol, evaluate in two separate studies the usefulness for the control of gastric adenocarcinoma of adriamycin (ADR)/5-fluorouracil (5-FU) vs. a 3-drug combination: BCNU/ADR/ftorafur in the U.S. study and mitomycin-C (MITO)/ADR/ftorafur in the Japanese study.

II. Establish the effectiveness of these regimens by evaluating the objective response rate, the duration of noted remissions and the survival time.

III. Compare the U.S. and Japanese data for the common Arm, adjusting for dosage differences.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with biopsy-proven metastatic adenocarcinoma of the stomach, incurable by surgery. Patients must have adequate hepatic, renal and bone marrow functions, a Karnofsky performance status of less than 40% and must not have had prior chemotherapy with adriamycin, 5-fluorouracil, ftorafur, mitomycin-C or BCNU, (as per addendum of July 1978).

PROTOCOL OUTLINE: Randomized study.

In the U.S., patients are randomized to Arm I or Arm II, in Japan patients are randomized to Arm III or Arm IV, and there are separate randomizations for Japanese patients with Karnofsky performance scores of 40 to 70% vs. those in the 80 to 100% category.

Arm I: NCOG. 3-Drug Combination Chemotherapy. BCNU, NSC-409962; Adriamycin, ADR, NSC-123127; Ftorafur, NSC-148958.

Arm II: NCOG-Common. 2-Drug Combination Chemotherapy. ADR; 5-Fluorouracil, 5-FU, NSC-19893.

Arm III: Japan-Common. 2-Drug Combination Chemotherapy. ADR; 5-FU.

Arm IV: Japan. 3-Drug Combination Chemotherapy. ADR; Mitomycin-C, MITO, NSC-26980; Ftorafur

STRATIFICATION BY: U.S. study: participating institutions, measurable vs. non-measurable disease, prior radiotherapy vs. no prior radiotherapy, resected vs. nonresected tumor, weight loss within last 2 months. In both U.S. and Japan: Karnofsky performance status: 40 to 70 vs. 80 to 100.

SPECIAL STUDY PARAMETERS: Liver and bone scans, upper GI or endoscopy, rectal examination.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, duration of remission, disease-free interval, patterns of recurrence.

CURRENT STATUS: 140 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: BCNU - 100 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 1; Ftorafur - 2 mg/sqm iv on days 1 and 2. Repeat course q 28 days. Discontinue ADR if bilirubin exceeds 3 mg%. Whem maximum cumulative dose of ADR (500 mg/sqm) is reached, and the patient still has significant clinical response, give additional therapy: BCNU - 150 mg/sqm iv on day 1; 5-FU - 325 mg/sq/day iv push on days 1 through 5. Repeat this course q 5 weeks.

Arm II: ADR - 50 mg/sqm iv on day 1; 5-FU - 500 mg/sqm iv on days 1, 2 and 3. Repeat course q 21 days. Discontinue ADR and give additional therapy as in Arm I, with BCNU, 5-FU.

Arm III: ADR - 35 to 50 mg/sqm iv on day 1; 5-FU - 350 to 500 mg/sqm iv on days 1, 2 and 3. Repeat course q 21 days. Discontinue ADR as in Arm I and give additional therapy: BCNU - 100 to 150 mg/sqm iv on day 1; 5-FU - 325 mg/sqm/day iv push on days 1 through 5. Repeat this course q 5 weeks.

Arm IV: ADR - 20 to 30 mg/sqm iv on day 1 q 21 days; MITO - 2.7 to 4 mg/sqm iv on day 1 q 7 days; Ftorafur - 534 mg/sqm/day po in 2 divided doses or 333 mg/sqm/day rectally (if oral dose not tolerated). Discontinue ADR and give additional therapy as in Arm III, with BCNU, 5-FU.

Increase dosage of all agents by 20% in Arms I and II, by 5 to 20% in Arms III and IV if no significant hematologic toxicity is noted. Continue therapy on all Arms for 2 years, then re-evaluate patient. Discontinue therapy and consider second-look laparotomy, if no evidence of disease. Continue therapy for patients with static disease. Remove from study patients with disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules; BCNU - 100 mg vials; 5-FU - 500 mg ampules; Ftorafur - 500 mg and 2 gm vials; Mitomycin-C - 5 mg vials.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00050378

2.0024 PHASE III ADJUVANT CHEMOTHERAPY WITH FAM (5-FU/ADR/MITO) VS SURGERY ALONE FOR LOCALLY ADVANCED GASTRIC ADENOCARCINOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7804

OBJECTIVES:

I. Determine the efficacy of adjuvant chemotherapy with FAM: 5-fluorouracil (5-FU), adriamycin (ADR), and mitomycin-C (MITO) on the disease-free interval and survival of patients with TNM Stage/Groups IB, IC, II and III gastric adenocarcinoma compared to results with potentially curative surgery alone.

PROTOCOL ENTRY CRITERIA: Patients with TNM Stage/Groups IB, IC, II or III gastric adenocarcinoma without gross or microscopic residual tumor postoperatively. Patients must not have had prior chemotherapy or radiotherapy; they must have wbc above 4000, platelets above 100,000, creatinine clearance more than 75 cc/minute, BUN not above 25 mg%, serum creatinine less than 1.5 mg%, serum bilirubin less than 2.0 mg/100 ml, SGOT and SGPT less than 3 times the upper limit of normal values.

PROTOCOL OUTLINE: Randomized study, following curative resection.

Arm I: No further therapy.

Arm II: 3-Drug Combination Chemotherapy. FAM: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Participating institutions; TNM Stage/Group: IB vs. IC vs. II vs. III.

SPECIAL STUDY PARAMETERS: CEA, upper GI series, LFT, liver scan.

END POINTS: Response/remission rate, disease-free interval, disease-free survival rate.

CURRENT STATUS: About 126 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

Arm I: No therapy.

Arm II: Begin 4 to 8 weeks following Surgery. 5-FU - 600 mg/sqm iv on days 1, 8, 29 and 36; ADR - 30 mg/sqm iv on days 1 and 29; MITO -10 mg/sqm iv on day 1. Repeat course q 8 weeks for a total of 6 courses (total ADR dose - 360 mg/sqm). Follow up all patients q 6 months for five years, then annually.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; ADR - 10 and 50 mg ampules; MITO - 5 mg vials.

DATE SUMMARIZED: 06/78

PATIENT ACCRUAL: 00160179

2.0025 PHASE II-III FAM (5-FU/ADR/MITO) VS V-FAM (FAM/VCR) VS CHLOROZOTOCIN CHEMOTHERAPY FOR ADVANCED GASTRIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) SWOG-7841

OBJECTIVES:

I. Determine whether vincristine (VCR) increases the effectiveness (as determined by response rate and survival) of FAM: 5-fluorouracil (5-FU)/mitomycin-C (MITO)/adriamycin (ADR) in the treatment of advanced, previously untreated gastric adenocarcinoma. (FAM alone treatment arm closed. Amendment 1, October 1979.)

II. Determine the efficacy as indicated by response rate and survival of chlorozotocin in the treatment of previously untreated gastric adenocarcinoma.

III. Determine by crossover, after relapse or failure on FAM, V-FAM or chlorozotocin, the effectiveness, as indicated by response rate and survival, of the alternate treatment in advanced gastric adenocarcinoma with prior therapy.

IV. Determine the toxicities of such treatments.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven advanced gastric adenocarcinoma, Stage IV (measurable disease, Amendment 1, October 1979), previously untreated by chemotherapy. Patients must have recovered from toxicity of any prior radiotherapy, which must have terminated at least 4 weeks before study entry. Patients must have a minimum life expectancy of 6 weeks, a performance status of 0 to 3, adequate hematologic function, serum creatinine within institutional norms and adequate cardiac function for Arms I and II.

PROTOCOL OUTLINE: Randomized study. Randomize patients without measurable disease to Arms I and II only. (All patients must have measurable disease. Amendment 1, October 1979.) Cross over nonresponders in Arms I or II to Arm III, Arm III failures to Arm I.

Arm I: 3-Drug Combination Chemotherapy. FAM: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980. (Arm closed. Amendment 1, October 1979.)

Arm II: 4-Drug Combination Chemotherapy. V-FAM: Vincristine, VCR, NSC-67574; 5-FU; ADR; MITO.

Arm III: Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

STRATIFICATION BY: Performance status: 0 and 1 vs. 2 and 3; measurable disease: yes or no; participating institutions.

SPECIAL STUDY PARAMETERS: CEA, liver scan, 2-hour pc glucose.

END POINTS: Response/remission rate, objective tumor response, response rate, survival time, toxicity/morbidity of treatment, alternate treatment response.

CURRENT STATUS: 35 patients will be entered to Arm III; at least 122 patients will be entered to Arms I and II.

DOSAGE SCHEDULE:

Arm I: FAM: 5-FU - 600 mg/sqm iv on days 1 and 8, 29 and 36 if wbc is above 3000; ADR - 30 mg/sqm (reduce dose by 50% if serum bilirubin is 1.3 to 3 mg/dl; maximum cumulative dose 450 mg/sqm) iv on day 1 and on day 29 if wbc is above 3000; MITO - 10 mg/sqm iv on day 1 only. (Arm closed. Amendment 1, October 1979.)

Arm II: V-FAM: VCR - 1.4 mg/sqm (maximum dose 2 mg) iv on days 1 and 8, and on days 29 and 36 if wbc is above 3000; 5-FU, ADR, and MITO, as in Arm I.

Repeat courses in Arms I and II q 8 weeks, but hold drugs for hematologic recovery as indicated. Cross over patients with intolerable toxicity or those failing to respond, or relapsing after response to Arms I or II to Arm III when 8 weeks have elapsed after the last MITO therapy and patient has recovered from toxicity. For these patients reduce dose of CLZ as indicated, and give CLZ q 6 weeks as tolerated.

Arm III: CLZ - 225 mg/sqm (175 mg/sqm for crossover patients with adequate bone marrow recovery, 120 mg for patients with damaged bone marrows) iv on day 1 q 6 weeks. Cross over patients with intolerable toxicity, or those failing to respond or relapsing after initial response to Arm I six weeks after the last CLZ dose. Modify FAM dosages for patients with myelosuppression.

Continue therapy in all arms for responders or patients with stable disease. Remove from study patients with progressive disease or relapse after 1 or more courses of crossover therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; MITO - 5 mg vials; 5-FU - 500 mg ampules; VCR - 1 and 5 mg vials; CLZ - 50 mg vials.

DATE SUMMARIZED: 04/80

2.0026 5-FU/MECCNU VS 5-FU/ADR/MECCNU AS ADJUVANT CHEMOTHERAPY FOLLOWING CURATIVE RESECTION FOR GASTRIC CANCER

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PROTOCOL NUMBER(S) GTSG-8180

OBJECTIVES:

I. Compare 5-fluorouracil (5-FU)/methyl-CCNU (MeCCNU) with 5-FU/MeCCNU/adriamycin as adjuvant chemotherapy following curative gastric resection in the treatment of gastric carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with stomach adenocarcinoma who have undergone resection with the removal of all known tumor. The tumor must have arisen in the stomach or in the cardioesophageal region, including the gastric mucosa in the distal esophagus. There may be no malignant cells in ascitic fluid, and peritoneal seeding may not have occurred. There may be no recent history of another neoplasm, except for basal cell carcinoma and in situ carcinoma of the cervix. Patients must be free from any infectious process, and bone marrow function must be adequate.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Methyl-CCNU, MeCCNU, NSC-95441.

Arm II: 3-Drug Combination Chemotherapy. 5-FU; Adriamycin, ADR, NSC-123127; MeCCNU.

STRATIFICATION BY: Participating institutions, extent of surgery (total and proximal resection vs. distal subtotal resection), lymph node status (positive vs. negative), depth of tumor invasion (invasion through the serosa or beyond vs. a lesser degree of invasion).

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, EKG, chest x-ray, cardiac ejection, CEA.

END POINTS: Disease-free interval, survival time, clinical suspicion of recurrence or metastases.

CURRENT STATUS: 100 patients are expected to be entered on each arm over 3.5 years.

DOSAGE SCHEDULE:

Arm I: 5-FU - 325 mg/sqm/day iv on days 1 through 5 and 375 mg/sqm/day iv on days 36 through 40; MeCCNU - 150 mg/sqm po on day 1 (maximum total dose 1 g/sqm). Repeat course q 10 weeks for 18 months.

Arm II: 5-FU - 325 mg/sqm/day iv on days 1 through 5 q 5 weeks; ADR - 40 mg/sqm iv push on day 1 q 5 weeks (maximum total cumulative dose 320 mg/sqm); MeCCNU - 110 mg/sqm po on day 1 q 10 weeks.

Chemotherapy in both arms to begin within 3-6 weeks of surgical resection and to continue for 18 months. Thereafter, patients will be followed for at least 10 years or until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; ADR - 10 and 50 mg vials; MeCCNU - 10, 20, 50, and 100 mg capsules.

DATE SUMMARIZED: 12/80

2.0027 PHASE II-III STUDY WITH 5-FU/ICRF-159/MECCNU, 5-FU/ADR WITH OR WITHOUT MITO OR MECCNU, AND 5-FU/MECCNU FOR UNRESECTABLE GASTRIC CANCER

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PROTOCOL NUMBER(S) GTSG-8376; MAYO-764101

OBJECTIVES:

I. Compare four regimens: FIMe (5-FU/ICRF-159/MeCCNU) vs. FAM (5-FU/ADR/MITO) vs. FAMe (5-FU/MeCCNU/ADR) vs. 5-FU/MeCCNU (Addendum, September 1976) for their effectiveness against advanced nonresectable gastric carcinoma. For the September 1978 Revision of this study, see GTSG-8376.

PROTOCOL ENTRY CRITERIA: Histologically proven residual, recurrent, or metastatic primary gastric adenocarcinoma with measurable tumor parameters. Allow three weeks minimum recovery interval following any major surgical procedure involving resection or bypass, two weeks from exploration and biopsy only, and 4 weeks from any previous radiation or chemotherapy. Patients with locally unresectable disease may be entered, patients with heart disease or prior chemotherapy are no longer eligible, Addendum 5, September 1970.

PROTOCOL OUTLINE: Randomized study.

Induction:

Randomize patients previously treated with ADR to Arms I and IV only. Randomize patients previously treated with MITO to Arms I, III or IV. Randomize patients with active heart disease and no prior therapy with 5-FU, ICRF-159 or MeCCNU to Arms I or IV. Assign patients with prior nitrosourea therapy to Arm II. Arm IV is to be assigned less frequently, using an imbalanced randomization assignment ratio of 3:3:3:2.

Arm I: 3-Drug Combination Chemotherapy. FIMe: 5-Fluorouracil, 5-FU, NSC-19893; ICRF-159, NSC-129943; Methyl CCNU, MeCCNU, NSC-95441. (Arm closed, Addendum 5, September 1978.

Arm II: 3-Drug Combination Chemotherapy. FAM: 5-FU; Adriamycin, ADR, NSC-123127; Mitomycin-C, NSC-26980. (Arm closed for locally unresectable patients, Addendum 1, January 1979).

Arm III: 3-Drug Combination Chemotherapy. FAMe: 5-FU; ADR; MeCCNU.

Arm IV: 2-Drug Combination Chemotherapy. 5-FU; MeCCNU. (Arm deleted Addendum, 5, September 1978, reopened for locally unresectable patients, Addendum, 2, January 1979.

Arm IVA: 2-Drug Combination Chemotherapy. 5-FU, ADR. (Arm added, Addendum 5 September, 1978). Enter 2 patients to each patient entered in Arms II and III.

Maintenance: Enter patients responding to Induction therapy.

Arm V: Enter responders to Arm I. Alternate 3-Drug Combination Chemotherapy with 2-Drug Combination Therapy. 5-FU, ICRF-159, MeCCNU alternating with ICRF-159, 5-FU.

Arm VI: Enter responders to Arm II. Alternate 3-Drug Combination Chemotherapy with 2-Drug Combination Therapy. 5-FU, ADR, MITO alternating with 5-FU, ADR.

Arm VII: Enter responders to Arm III. Alternate 3-Drug Combination Chemotherapy with 2-Drug Combination Chemotherapy. 5-FU, MeCCNU, ADR alternating with 5-FU, ADR.

Arm VIII: Enter responders to Arm IV. 2-Drug Combination Chemotherapy. 5-FU, MeCCNU.

STRATIFICATION BY: Disease stage: locally unresectable vs. measurable vs. nonmeasurable; chemotherapy - no prior chemotherapy, chemotherapy with non-study agents, chemotherapy with study agents; heart disease -absent, present; status of primary tumor - present, resected; performance status (ECOG Scale) - 0 to 1, 2 or 3; liver involvement (Addendum 5, September 1978).

SPECIAL STUDY PARAMETERS: Immunologic determinants, liver scans, tumor measurements, performance status (ECOG scale symptomatic status).

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response.

CURRENT STATUS: 260 patients will be entered in approximately 2 years. Study revised September 1978; see GTSG-8376R.

DOSAGE SCHEDULE:

Induction:

Arm I: 5-FU - 325 mg/sqm/day rapid iv push, on days 1 through 5 and days 36 through 40; ICRF-159 - 500 mg/sqm/day po x 3 days on days 2 through 4, and 36 through 38; MeCCNU - 110 mg/sqm po on day 1. Repeat course q 10 weeks. (Arm deleted September 1978).

Arm II: 5-FU - 275 mg/sqm/day rapid iv push x 5 days on days 1 through 5 and 36 through 40; ADR - 30 mg/sqm/day rapid iv push on day 1 and day 36; MITO-C - 10 mg/sqm rapid iv push on day 1. Reduce ADR dose to 20 mg/sqm if jaundice is present, and limit total ADR dose to 550 mg. Repeat course q 10 weeks. (Arm closed to locally unresectable disease, Addendum 1, January 1979).

Arm III: 5-FU - 275 mg/sqm (325 mg/sqm iv on days 1 through 5 q 5 weeks Addendum 1, January 1979). Rapid iv push x 5 days on days 1 through 5 and 36 through 40; MeCCNU - 100 mg/sqm (110 mg/sqm Addendum 1, January 1979) po on day 1 and repeat q 10 weeks; ADR - 40 mg/sqm iv on days 1 and 36 and repeat q 5 weeks. Reduce ADR to 25 mg/sqm if jaundice is present.

Arm IV: 5-FU - 300 mg/sqm/day (325 on days 1 through 5, 375 on days 36 through 40 for locally unresectable patients) rapid iv push x 5 days on days 1 through 5; MeCCNU - 175 mg/sqm (150 mg/sqm on day 1 q 10 weeks for locally unresectable patients) po on day 1. Evaluate at 7 weeks. Remove nonresponders from study. Repeat course q 7 weeks for patients with objective response or no change. If wbc is less than 4,000 and platelets less than 150,000 at 7 weeks withhold MeCCNU, continue 5-FU alone given q 5 weeks (Addendum 4, September 1977).

Arm IVA: 5-FU - 350 mg/sqm iv on days 1 through 5 q 5 weeks; ADR -50 mg/sqm on day 1 q 5 weeks. After a total ADR dose of 550 mg/sqm, continue therapy with FU alone: 500 mg/sqm on days 1 through 5 q 5 weeks.

Maintenance:

Remove from study all patients in Arms I, II and III who show objective progression after 5 weeks, and all nonresponders in Arm IV after 7 weeks.

Arm V: Alternate Arm I chemotherapy with 5-FU, ICRF-159, MeCCNU with 5-FU, ICRF-159 q 5 weeks. Repeat course q 10 weeks.

Arm VI: Alternate Arm II chemotherapy with 5-FU, ADR, MITO with 5-FU, ADR q 5 weeks. Repeat course q 10 weeks.

Arm VII: Alternate Arm III chemotherapy with 5-FU, MeCCNU, ADR with 5-FU-ADR q 5 weeks. Repeat course q 10 weeks.

Arm VIII: Repeat Arm IV induction course with 5-FU, MeCCNU q 7 weeks.

DOSAGE FORMS: MITO-C - 5 mg vials; ADR - 10 and 20 mg vials; MeCCNU - 10, 20, 50, and 100 mg capsules; ICRF-159 - 50, 250, and 500 mg tablets; 5-FU - available in standard marketed form.

DATE SUMMARIZED: 05/79

PATIENT ACCRUAL: 02421276

2.0028 PHASE II-III COMBINATION CHEMOTHERAPY WITH 5-FU/ADR WITH OR WITHOUT MECCNU OR MITO FOR UNRESECTABLE GASTRIC CANCER

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PROTOCOL NUMBER(S) GTSG-8376R

OBJECTIVES:

I. Compare chemotherapy with FAMe - 5-fluorouracil (5-FU)/adriamycin (ADR)/methyl CCNU (MeCCNU) vs. FAM - 5-FU/ADR/mitomycin C (MITO) vs. 5-FU/ADR alone for unresectable advanced gastric cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven residual, recurrent, or metastatic and nonresectable primary gastric adenocarcinoma. Patients must have measurable tumor parameters, except patients with nonmetastatic locally advanced disease. Patients must have an ECOG Performance Status better than 4, adequate hematologic status, nutrition and food intake, no prior Chemotherapy, no active heart disease, and no prior Radiotherapy to indicator lesions. Allow three weeks minimum recovery interval following any major surgical procedure involving resection or bypass, two weeks from exploration and biopsy only, and four weeks from any previous radiation.

PROTOCOL OUTLINE: Randomized study. Enter 2 patients to Arm III for every 1 patient entered to Arms I and II.

Arm I: 3-Drug Combination Chemotherapy. FAMe - 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Methyl CCNU, MeCCNU, NSC-95441.

Arm II: 3-Drug Combination Chemotherapy. FAM - 5-FU; ADR; plus Mitomycin C, MITO, NSC-26980.

Arm III: 2-Drug Combination Chemotherapy. 5-FU; ADR.

STRATIFICATION BY: Participating institutions; disease stage: local microscopic vs. local macroscopic vs. advanced measurable vs. advanced nonmeasurable; performance status: ECOG 0 vs. 1 vs. 2 or 3.

SPECIAL STUDY PARAMETERS: CEA, tumor measurements, liver scan if indicated.

END POINTS: Objective tumor response, response rate, time to progression, survival time, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 120 patients will be entered in 1 year.

DOSAGE SCHEDULE: Enter patients with locally nonresectable disease between 3 and 6 weeks following surgery.

Induction and Maintenance:

Arm I: FAMe: 5-FU - 325 mg/sqm/day iv on days 1 through 5 and 36 through 40 q 5 weeks; MeCCNU - 110 mg/sqm po on day 1 and q 10 weeks; ADR - 40 mg/sqm (maximum cumulative dose 550 mg/sqm) iv on days 1 and 36 and q 5 weeks.

Arm II: FAM: 5-FU - 275 mg/sqm iv on days 1 through 5, 36 through 40, and q 5 weeks; ADR - 30 mg/sqm iv on days 1 and 36 and q 5 weeks; MITO - 10 mg/sqm iv on day 1 q 10 weeks.

Arm III: 5-FU - 350 mg/sqm iv on days 1 through 5; ADR - 50 mg/sqm on day 1. Repeat course q 5 weeks.

Remove from study patients in any Arm with disease progression after 5 weeks of therapy, and follow up all patients for survival. Continue therapy for patients who remain stable or show objective regression. When maximum dose of ADR has been given, continue therapy with remaining drugs.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MITO - 5 mg vials; ADR - 10 and 20 mg vials; MeCCNU - 10, 20, 50, and 100 mg capsules; 5-FU - not given.

DATE SUMMARIZED: 05/79

2.0029 PHASE II CHEMOTHERAPY WITH MTX, ICRF-159, TRIAZINATE, AND HIGH-DOSE MTX/CF RESCUE FOR ADVANCED GASTRIC CANCER

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PROTOCOL NUMBER(S) GTSG-8477

OBJECTIVES:

I. Determine the quantitative response rate of gastric cancer to four single agents: standard-dose methotrexate, high-dose methotrexate with citrovorum rescue, triazinate (Baker's Antifol), and ICRF-159.

II. Determine if a dose escalation from standard- to high-dose methotrexate will increase the ability to achieve response.

III. Compare the primary response rates for three antifolic compounds.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed measurable disease of residual, recurrent or metastatic gastric adenocarcinoma not amenable to surgical cure, who have had no major surgery within 3 weeks, no minor surgery within 2 weeks, and no prior radiotherapy or chemotherapy within 4 weeks. Prior chemotherapy must not have been with study agents other than ICRF-159, performance status must be less than 4. Patients must have adequate hematologic, creatinine and bilirubin values, adequate nutrition and no third space or fluid overloaded circumstance.

PROTOCOL OUTLINE: Randomized study.

Enter patients previously treated with 5-FU, who have kidney disease to Arm IV only. (Arm IV discontinued. Randomize patients to Arm II or III. Addendum 4, June 1980). Randomize patients with prior ICRF therapy to Arms I, II or III only. Institutions may elect randomization to Arms II, III and IV only. (Randomize patients with bilirubin above 1.5 mg% to Arms I, III and IV only. Addendum 2, January 1978)

Arm I: 2-Drug Combination Chemotherapy. High-dose Methotrexate, MTX, NSC-740; plus rescue with Citrovorum Factor, CF, NSC-3590. (Arm discontinued; patients randomized to Arm II, III, or IV. Addendum 3, October 1979.)

Arm II: Single-agent Chemotherapy. Baker's Antifol, TZT, NSC-139105.

Arm III: Single-agent Chemotherapy. MTX, in conventional doses.

Arm IV: Single-agent Chemotherapy. ICRF-159, NSC-129943. (Arm discontinued. Addendum 4, June 1980)

STRATIFICATION BY: Participating institutions: randomizing to 3 vs. 4 arms; performance status: 0-1 vs. 2-3; kidney diseases vs. none; bilirubin: more vs. less than 1.5 mg% (Addendum 2, January 1978); prior therapy: prior ICRF-159 vs. prior radiation and/or chemotherapy without prior ICRF-159 vs. no prior radiation or chemotherapy.

SPECIAL STUDY PARAMETERS: IVP and creatinine clearance prior to randomization; immunologic determinants.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, response duration.

CURRENT STATUS: About 80 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

Arm I: Hydrate patient and maintain urine alkalinity above pH 7. MTX - 3 gm/sqm iv. 24 hours later, if MTX blood level is not above 5.0 times 10 to the minus 6, and serum creatinine increase is not more than 50%, give CF - 10 mg/sqm iv, then 10 mg/sqm q 6 hours for 12 doses. If MTX and creatinine levels are above these values, call study chairman and give CF - 100 mg po q 3 hours for 48 doses or until MTX level is less than 5.0 times 10 to the minus 6. Maximum total rescue period is 96 hours. Repeat course q 7 days for 4 weeks, then q 14 days for 4 weeks. If no objective response at 12 weeks, discontinue therapy. (Arm discontinued. Addendum 3, October 1979.)

Arm II: TZT - 250 mg/sqm/day iv on days 1, 2 and 3 q 3 weeks.

Arm III: MTX - 40 mg/sqm iv bolus q 7 days.

Arm IV: (Arm discontinued. Addendum 4, June 1980). ICRF-159 - 900 mg/sqm/day po in 3 divided doses on days 1, 2 and 3 q 4 weeks. Remove from study patients developing unacceptable toxicity or progressive disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TZT - 100 and 250 mg vials; ICRF-159 - 50 and 500 mg tablets; MTX - 50 and 500 mg vials.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00251278

2.0030 ADJUVANT CHEMOTHERAPY WITH 5-FU/ADR FOLLOWING CURATIVE SURGERY FOR ADENOCARCINOMA OF THE STOMACH

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PROTOCOL NUMBER(S) MAYO-794151; NCCTG-794151

OBJECTIVES:

I. Determine whether adjuvant combination chemotherapy with 5-fluorouracil (5-FU)/adriamycin (ADR) substantially improves the cure rate following potentially curative surgery for adenocarcinoma of the stomach.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed primary adenocarcinoma of the stomach treated surgically with curative intent. Patients must: be fully recovered from surgery, be ingesting at least 1500 calories a day, be between 4 to 6 weeks beyond surgery, and have an ECOG performance status of at least 2. Patients must not have: tumor at line of resection, tumor that cannot be excised en bloc, gastric carcinoma that has not invaded the muscularis, radiation to more than 15 percent of the bone marrow within preceeding 30 days or to more than 30 percent at any time if dose was 2500 rads or more in 13 fractions, leukopenia, or jaundice.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. 5-Flurorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127.

Arm II: No Chemotherapy.

STRATIFICATION: Extent of gastrectomy: total vs. subtotal; site of primary: cardia vs. diffuse vs. all others; Dukes stage: B1 vs. B2 vs. C1 vs. C2.

SPECIAL STUDY PARAMETERS: Liver and kidney function.

END POINTS: Recurrence rate, length of survival.

CURRENT STATUS: 126 patients will be entered in 3 years.

DOSAGE SCHEDULE: Randomize patients between 4 to 6 weeks after surgery.

Arm I: 5-FU - 350 mg/sqm iv on days 1 through 5; ADR - 50 mg/sqm iv on day 1 of 5-FU; q 5 weeks for 3 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 10 ml ampules; ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 02/80

2.0031 PHASE II TRIAL OF ICRF-159 IN THE TREATMENT OF ADVANCED GASTRIC CARCINOMA

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PROTOCOL NUMBER(S) NCI-77-C-67; NCI-VA-MOB-7617

OBJECTIVES:

I. Determine the antitumor activity of ICRF-159 in patients with advanced gastric adenocarcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented adenocarcinoma of the stomach that is not amenable to curative surgery. Patients must have an evaluable lesion. Patients may have relapsed after or failed to respond to radiotherapy. Patients must have a life expectancy of at least one month and must not be completely bedridden. Bone marrow function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. ICRF-159, NSC-129943.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, total proteins, albumin, CEA, AFP, upper GI series, gastroscopy, liver scan, liver biopsy if used as evaluable lesion.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

ICRF-159 - 3 g/sqm in 3 divided doses po. Repeat weekly. Responding patients and those with stable disease continue on treatment until progressive disease develops.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ICRF - 50 and 250 mg tablets.

DATE SUMMARIZED: 08/80

2.0032 SURGERY PLUS INTRAOPERATIVE RADIOTHERAPY WITH RADIOSENSITIZATION VS SURGERY ALONE FOR ADENOCARCINOMA OF THE STOMACH

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PROTOCOL NUMBER(S) NCI-80-C-59; NCI-ROB-802

OBJECTIVES:

I. Assess the technical feasibility of delivering intraoperative electron radiotherapy combined with radical surgery in the treatment of adenocarcinoma of the stomach.

II. Assess the role of intraoperative radiotherapy as an adjunct to surgical resection for the local control and survival of patients with resectable gastric adenocarcinoma.

III. Compare the efficacy of intraoperative and conventional radiotherapy for the local control and survival of patients with marginally resectable gastric cancers or with gross residual tumor remaining after resection.

IV. Evaluate and compare the acute and delayed morbidities of intraoperative and conventional external beam radiotherapy to the gastric area.

V. Evaluate misonidazole as a hypoxic cell sensitizer at the time of intraoperative radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed adenocarcinoma of the stomach who have no evidence of metastatic disease beyond the regional lymph nodes and who have received no significant previous radiotherapy or chemotherapy. Patients must be between the ages of 18 and 75 years. Patients with previous gastrectomy must have had pathologically positive margins for tumor and must be within 4 months of original surgery. Patients may enter study if they have locally recurrent tumor after prior surgical resection.

PROTOCOL OUTLINE: Randomized study.

Arm I: Control. Surgery with or without Conventional External Beam Photon Radiotherapy.

Arm II: Surgery with Intraoperative Radiotherapy and Radiosensitization. 6 MeV electrons; Misonidazole, MNI, NSC-261037.

STRATIFICATION BY: Primary tumor vs. recurrence after previous resection; referral prior to any surgical exploration vs. referral after surgical exploration; weight loss (15 percent or more of body weight vs. less than 15 percent).

SPECIAL STUDY PARAMETERS: Hemogram, electrolytes, chemistry panel, blood sugar, kidney and liver function tests, CEA, chest x-ray, full-lung tomograms, barium swallow, abdominal CAT, abdominal ultrasound, liver scan, endoscopy.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment, disease-free interval.

CURRENT STATUS: About 99 patients will be entered in 5 years.

DOSAGE SCHEDULE:

Arm I: Patients resected for cure receive surgical resection alone. Those who are marginally resectable or with residual disease receive resection or debulking plus postoperative conventional external beam Radiotherapy beginning when the surgical wound has healed: 4500 rads in 180-rad fractions, 5 fractions/week, to the area of the primary tumor mass and all structures at risk for recurrence. An additional 1000 rads may be delivered to a reduced volume if appropriate.

Arm II: All patients (resectable for cure, marginally resectable, and residual disease) receive intraoperative electron Radiotherapy: 2000 rads in no more than 10 minutes. MNI - 3.5 g/sqm iv over 5 minutes 15 minutes prior to Radiotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

2.0033 COMBINATION CHEMOTHERAPY WITH 5-FU/ADR/MITO FOR NONRESECTABLE GASTRIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) BRA-10275-TP-ACG-1

OBJECTIVES:

I. Determine the efficacy in terms of response, duration of remission and survival, of FAM: 5-fluorouracil (5-FU)/adriamycin (ADR)/mitomycin-C (MITO) in the treatment of advanced gastric carcinoma.

II. Define the quantitative and qualitative toxicity of this regimen.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven gastric adenocarcinoma not amenable to surgery. Disease must not involve regional lymph nodes. Patients must have adequate oral nutrition and cardiac and hematologic status. Patients must have an ECOG performance status less than 4 and have had no prior 5-FU therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 3-Drug Combination Chemotherapy. FAM: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980.

Maintenance: 3-Drug Combination Chemotherapy. 5-FU, ADR, MITO.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hepatic function.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, duration of remission, survival rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: FAM: 5-FU - 275 mg/sqm iv on days 1 through 5 and 36 through 40; ADR - 30 mg/sqm (maximum cumulative dose 550 mg/sqm) iv on days 1 and 36; MITO - 10 mg/sqm iv on day 1. Repeat course q 10 weeks.

Evaluate q 5 weeks. Patients with objective progression are off study; others enter Maintenance.

Maintenance: Alternate FAM as in Induction with 5-FU/ADR as in Induction until maximum ADR dose is reached. Then continue 5-FU and MITO, omitting ADR. Repeat course q 5 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

2.0034 PHASE II-III COMBINATION CHEMOTHERAPY WITH MEFA (ADR/5-FU/MECCNU) VS FA (ADR/5-FU) FOR ADVANCED GASTRIC CANCER

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PROTOCOL NUMBER(S) EORTC-40791

OBJECTIVES:

I. Compare MeFA (adriamycin/5-fluorouracil/methyl-CCNU) with FA (adriamycin/5-fluorouracil) for the treatment of advanced gastric cancer.

II. Assess the rate of objective response and the median survival time.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven, unresectable gastric cancer, measurable and/or non-measurable disease. Patients must be under 70 years of age and have adequate hematologic, renal and hepatic function; Karnofsky performance status must be at least 60. Patients must be able to take oral medication and must not have heart disease or a history of heart failure, active infection, CNS disease or prior chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. MeFA: Methyl-CCNU, MeCCNU, NSC-95441; 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, 123127.P

Arm II: 2-Drug Combination Chemotherapy. FA: ADR, 5-FU.

STRATIFICATION BY: Measurable disease: yes vs. no; participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic, renal and hepatic function tests.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, duration of response, survival rate, length of survival.

CURRENT STATUS: Approximately 100 patients (50 in each arm) will be entered.

DOSAGE SCHEDULE:

Arm I: MeFA: MeCCNU - 150 mg/sqm po on day 1 q 10 weeks; 5-FU - 300 mg/sqm iv on days 1 through 5 q 5 weeks; ADR - 40 mg/sqm iv running solution on day 1 q 5 weeks, for a total ADR dose of 550 mg/sqm.

Arm II: FA: ADR - 50 mg/sqm iv running solution on day 1 q 5 weeks for a total dose of 550 mg/sqm; 5-FU - 350 mg/sqm iv on days 1 through 5 q 5 weeks.

Treatment is continued until progression of disease or until the life of the patient is endangered.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 250 mg ampules; ADR - 10 mg ampules; MeCCNU - 10, 50 and 100 mg capsules.

DATE SUMMARIZED: 10/80

2.0035 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR RESISTANT GASTRIC CANCER

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PROTOCOL NUMBER(S) EORTC-40793

OBJECTIVES:

I. Study the clinical effects (assessed by the objective response rate and the duration of response) of cis-platinum on measurable gastric cancer resistant to previous chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven gastric cancer and measurable disease defined as follows: nodular pulmonary metastases not seen in previous chest x-rays, palpable supraclavicular lymph nodes and subcutaneous masses, hepatomegaly of more than 5 cm below the costal margin if proven to contain metastases, and abdominal masses where there are clear limits in the two largest perpendicular diameters. Patients must be under 70 years of age, have a Karnofsky performance status of 50 or more, and adequate renal function. Patients must have failed to respond to previous chemotherapy. Patients must have no severe malnutrition, malabsorption syndrome, severe nausea and vomiting, CNS disease, psychosis or other different primary tumor.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic and renal function tests, tumor measurements, hepatic function tests, general toxicity.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival.

CURRENT STATUS: Initially 20 patients will be treated; 5 patients will be added for each response, to a maximum of 50 patients.

DOSAGE SCHEDULE:

CACP - 100 mg/sqm iv in a 6-hour infusion with prehydration, 37.5 g mannitol diuresis, and intravenous furosemide to maintain hourly diuresis. Diuresis is maintained for 24 hours after CACP infusion. Repeat Chemotherapy q 3 weeks. Patients receive 2 courses of treatment; those with progressive disease go off study, and those showing remission continue treatment until relapse. Those showing no change continue treatment until remission or progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 and 25 mg vials.

DATE SUMMARIZED: 10/80

2.0036 PHASE II POSTOPERATIVE CHEMOTHERAPY WITH MITO/FT OR IMMUNOTHERAPY WITH OK-432 FOR CARCINOMA OF THE STOMACH

Nakazato, K., (Nagoya 052-762-6111) Aichi Cancer Center Hospital, 81-1159 Kanokoden, Tashiro-cho, Chikusa-ku, Nagoya 464, Japan
PROTOCOL NUMBER(S) JAP-ACC-102

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with mitomycin-C/ftorafur or immunotherapy with OK-432 in patients who have undergone curative surgery for carcinoma of the stomach.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven primary adenocarcinoma of the stomach who have been treated surgically with curative intent. Mucosal and submucosal cancers without lymph node metastases are excluded, as is cancer invasive to adjacent organs. Patients must be under 75 years of age and have a performance status of at least 80 percent. There must be adequate bone marrow, renal, and hepatic function.

PROTOCOL OUTLINE: Randomized study. All patients undergo curative surgery prior to randomization.

Arm I: 2-Drug Combination Chemotherapy. Mitomycin-C, MITO, NSC-26980; Ftorafur, FT, NSC-148958.

Arm II: Single-agent Immunotherapy. OK-432, NSC-293562.

Arm III: No further treatment.

STRATIFICATION BY: Performance status: equal to or less than 80 percent vs. above 80 percent; surgical status: curative vs. noncurative vs. nonresectable; serosal invasion: S0 vs. S1 and S2.

SPECIAL STUDY PARAMETERS: Skin tests: PPD, CT, CEA.

END POINTS: Actuarial survival time study, age-adjusted survival rate, disease-free interval, regression analysis, characterization between the interval and type of recurrences.

CURRENT STATUS: 100 patients will be entered yearly.

DOSAGE SCHEDULE:

Arm I: MITO - 0.08 mg/kg iv twice weekly during weeks 1 through 4 following Surgery; FT - 12 mg/kg/day po during weeks 4 to 8 after Surgery. Give drugs sequentially for 3 or 6 months.

Arm II: OK-432 - 0.5 KE ic q other day during hospitalization. Continue treatment q 1-2 weeks for 3 or 6 months. Dose may be increased from 1 to 5 KE.

Arm III: No further treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: MITO - 2 mg vials; FT - 200 mg capsules; OK-432 - 0.2, 0.5, 1, and 5 KE vials.

DATE SUMMARIZED: 12/80

2.0037 PHASE III ADJUVANT CHEMOTHERAPY WITH FT-207, IMMUNOTHERAPY WITH OK-432 ALONE OR COMBINED FOR NONOPERABLE CARCINOMA OF THE STOMACH

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PROTOCOL NUMBER(S) JAP-TSC-IC-CSG-3

OBJECTIVES:

I. Determine the efficacy of chemotherapy with ftorafur, immunotherapy with OK-432 or the combination of the modalities in patients with nonresectable carcinoma of the stomach.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with noncuratively resected gastric cancer. Results of laboratory tests must be adequate.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Immunotherapy plus Single-agent Chemotherapy. Picibanil, OK-432, NSC-293562; plus Ftorafur, FT-207, NSC-148958.

Arm II: Single-agent Immunotherapy. OK-432.

Arm III: Single-agent Chemotherapy. FT-207.

STRATIFICATION BY: Disease stage: noncurative resected vs. curative resected vs. nonresected; participating institutions.

SPECIAL STUDY PARAMETERS: Skin tests: PPD, PHA.

END POINTS: Remission interval, survival distribution, toxicity/morbidity of treatment.

CURRENT STATUS: 150 patients will be entered annually.

DOSAGE SCHEDULE:

Arm I: OK-432 - 2 to 5 KE ic q other day during hospitalization, beginning 2 weeks after Surgery. After release from hospital, patients continue treatment q week until relapse. FT-207 - 12 mg/kg/day po beginning 2 weeks after Surgery. Continue daily until relapse.

Arm II: OK-432 as in Arm I.

Arm III: FT-207 as in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: FT-207 - 200 mg capsules; OK-432 - 0.2, 0.5, 1, and 5 KE vials.

DATE SUMMARIZED: 12/80

2.0038 PHASE II CHEMOTHERAPY WITH VP-16 FOR ADVANCED GASTRIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) PERU-INEN-7707

OBJECTIVES:

I. Evaluate the effectiveness of VP-16 for remission induction in surgically noncurable gastric adenocarcinoma.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven gastric adenocarcinoma not curable by surgery. Patients must have no gastrointestinal obstructions, a minimum life expectancy of 6 weeks and adequate renal, hepatic, and bone marrow function.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: Single-agent Chemotherapy. VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: CEA, gastroscopy.

END POINTS: Objective tumor response, response/remission rate, relapse rate, duration of response, survival time.

CURRENT STATUS: 16-25 patients will be entered.

DOSAGE SCHEDULE:

Induction: Begin therapy within 2 to 4 weeks after diagnostic surgery. VP-16 - 180 mg/sqm iv on day 1. Repeat course q week for a minimum of 8 doses for an adequate trial. Remove patients with disease progression from study. Follow patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VP-16 - 20 mg ampules.

DATE SUMMARIZED: 12/78

2C. PANCREAS

2.0039 PHASE II CHEMOTHERAPY WITH FAM (5-FU/ADR/MITO) VS SMF (SZC/5-FU/MITO) FOR ADVANCED NONRESECTABLE PANCREATIC CANCER

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-7982

OBJECTIVES:

I. Compare effects of FAM - 5-Fluorouracil (5-FU)/Adriamycin (ADR)/Mitomycin-C (MITO) vs. SMF - Streptozotocin (SZC)/MITO/5-FU for advanced pancreatic carcinoma not amenable to curative surgery.

II. Compare psychological distress, particularly depression, of patients with unresectable pancreatic cancer vs. patients with locally advanced gastric cancer (CLB-7981).

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with histologically confirmed or strongly presumed (on basis of surgical inspection and biopsy of a metastatic lesion consistent with pancreatic primary plus either clearly defined defect consistent with a pancreatic primary on computerized tomography, sonography, angiogram, or pancreatic ductography or evidence of duodenal invasion consistent with pancreatic carcinoma on barium roentgenography) ductal, acinar, or undifferentiated adenocarcinoma of the pancreas which is not amenable to curative surgery. Patients must have an estimated survival time of at least 2 months, a performance scale of at least 3, adequate cardiac, bone marrow and kidney function, and caloric intake of at least 1200 calories/day. Patients must be at least 3 weeks beyond abdominal surgery, 2 weeks beyond abdominal exploration, and 4 weeks beyond radiotherapy. Patients must not have had prior chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. FAM: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980.

Arm II: 3-Drug Combination Chemotherapy. SMF: Streptozotocin, SZC, NSC-85998; 5-FU; MITO.

STRATIFICATION: Participating institutions; measurable vs. non-measurable disease; performance status: 0 or 1 vs. 2 or 3.

SPECIAL STUDY PARAMETERS: CEA; liver scan; bone and brain scans if indicated; echocardiogram.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival time, quality of survival.

CURRENT STATUS: 97 patients will be entered in 20 months.

DOSAGE SCHEDULE:

Arm I: 5-FU - 600 mg/sqm iv direct infusion days 1, 8, 29 and 36; ADR - 30 mg/sqm (maximum total dose 480 mg/sqm) iv direct infusion over 5 minutes on days 1 and 29; MITO - 10 mg/sqm iv direct infusion on day 1.

Arm II: SZC - 1.0 gm/sqm iv over 20 minutes on days 1, 8, 29 and 36; 5-FU and MITO - as in Arm I.

Repeat courses q 8 weeks and evaluate the patients after 2 courses. Remove from study patients in progression after 1 course or any time thereafter. Keep patients who respond or have stable disease after 1 course on study until disease progression or prohibitive toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

2.0040 PHASE II-III CHEMOTHERAPY WITH PALA VS COMBINATION CHEMOTHERAPY WITH SAM (STZ/ADR/MECCNU) FOR PANCREATIC CARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-2279

OBJECTIVES:

I. Allow for the evaluation of new agents or combinations in patients with untreated measurable carcinoma of the pancreas (master protocol).

II. Determine the rate of objective response and duration of survival of patients treated with SAM (streptozotocin/methyl-CCNU/adriamycin) for advanced measurable pancreatic adenocarcinoma.

PROTOCOL ENTRY CRITERIA: Patients with nonresectable, histologically proven pancreatic carcinoma; there must be a measurable area of known metastatic disease. Patients must have a life expectancy of more than 2 months and a performance status of 0, 1, 2, or 3. There must be no active infectious process, severe malnutrition, severe nausea, frequent vomiting, leukopenia, thrombocytopenia, renal disease with azotemia or significant impairment of liver function. Patients must have adequate cardiac status. Patients must have received no prior chemotherapy and no radiotherapy to the measurable lesions within the month prior to entry. No major surgical procedures (resection and anastomosis) are allowed within three weeks prior to entry, and no exploration or biopsy within two weeks prior to entry.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. PALA, NSC-224131.

Arm II: 3-Drug Combination Chemotherapy. SAM: Streptozotocin, STZ, NSC-85998; Adriamycin, ADR, NSC-123127; Methyl-CCNU, MeCCNU, NSC-95441.

STRATIFICATION BY: Performance status (ECOG): 0-1 vs. 2-3; grade of anaplasia: well differentiated (Broder's Grade I) vs. moderately undifferentiated (Broder's Grade II and III) vs. highly undifferentiated (Broder's Grade IV).

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; chest x-ray; liver, brain, bone marrow, and bone scans; EKG; ultrasound examination of upper abdomen.

END POINTS: Response/remission rate, objective tumor response, duration of survival.

CURRENT STATUS: An accrual of 50 evaluable patients per year is anticipated.

DOSAGE SCHEDULE:

Arm I: PALA - 1250 mg/sqm iv over 10 minutes daily for 5 days q 4 weeks. All patients receive at least 2 courses. Patients continue on therapy until disease progression or unmanageable toxicity.

Arm II: SAM: STZ - 400 mg/sqm iv on days 1 to 5 q 6 weeks; ADR - 45 mg/sqm rapid iv infusion on days 1 and 22 q 6 weeks to a maximum cumulative dose of 540 mg/sqm; MeCCNU - 60 mg/sqm po, preferably at bedtime, on day 1 q 6 weeks. When the maximum dose of ADR is reached, continue with STZ and MeCCNU. Patients continue on therapy until disease progression or unmanageable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 100 mg vials; STZ - 1 g vials; ADR - 10, 50, and 100 mg capsules and 100 mg vials.

DATE SUMMARIZED: 12/80

2.0041 PHASE II-III CHEMOTHERAPY WITH STREPTOZOTOCIN PLUS 5-FU OR ADR VS CHLOROZOTOCIN FOR METASTATIC ISLET CELL CARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-3278

OBJECTIVES:

I. Compare streptozotocin (SZC)/5-fluorouracil versus SZC/adriamycin in the treatment of metastatic islet cell carcinoma.

II. Test chlorozotocin (CLZ) alone in the treatment of islet cell carcinoma to determine whether this agent has activity unto itself and to determine whether there is any cross resistance with SZC.

PROTOCOL ENTRY CRITERIA: Patients with measurable, symptomatic or rapidly advancing, histologically proven islet cell carcinoma not amenable to surgery. Patients must have adequate nutrition, bone marrow, renal and hepatic function, and a performance status better than 4. Patients must not have had prior nitrosourea therapy other than SZC, chemotherapy or radiotherapy in the previous month, exploratory surgery or biopsy in the previous 2 weeks, nor surgical resection or anastomosis within 3 weeks.

PROTOCOL OUTLINE: Randomized study. Enter patients with prior SZC therapy to Arm III. Randomize patients previously treated with 5-FU alone to Arms II and III. Randomize patients with active heart disease or previously treated with ADR alone to Arms I and III.

Arm I: 2-Drug Combination Chemotherapy. Streptozotocin, SZC, NSC-85998; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 2-Drug Combination Chemotherapy. SZC; Adriamycin, ADR, NSC-123127.

Arm III: Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

STRATIFICATION BY: Participating institutions; performance status: 0-1 vs. 2-3; objective indicator: measurable tumor vs. endocrine function; prior chemotherapy: none vs. SZC vs. 5-FU alone vs. ADR alone; active heart disease.

SPECIAL STUDY PARAMETERS: Serum gastrin, blood insulin, weight and volume of 24-hour stool.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 84 patients will be entered.

DOSAGE SCHEDULE:

Arm I: SZC - 500 mg/sqm iv on days 1 through 5; 5-FU - 400 mg/sqm iv on days 1 through 5. Repeat course q 6 weeks until progression. Cross over patients with progressive disease to Arm III.

Arm II: SZC as in Arm I; ADR - 50 mg/sqm iv on days 1 and 22. Repeat course q 6 weeks until progression. Cross over patients with progressive disease to Arm III.

Arm III: CLZ - 150 mg/sqm iv on day 1. Repeat course q 7 weeks. Rerandomize patients with progressive disease to either Arm I or II if eligible. Enter patients with prior ADR therapy or active heart disease to Arm I upon progression. Enter patients with prior 5-FU therapy to Arm II upon progression. Remove patients with prior SZC therapy from study upon progression.

Evaluate all patients in Arms I and II q 6 weeks, all patients in Arm III q 7 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: SZC - 1 gm vials; ADR - 10 and 50 mg vials; 5-FU - 500 mg vials; CLZ - 50 mg vials.

DATE SUMMARIZED: 12/78

2.0042 PHASE III CHEMOTHERAPY WITH ADR/5-FU VS BCNU/ADR/FT FOR DISSEMINATED PANCREATIC CARCINOMA

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PROTOCOL NUMBER(S) NCOG-3P62

OBJECTIVES:

I. Compare the efficacy of adriamycin/5-fluorouracil vs. adriamycin/BCNU/ftorafur in patients with metastatic adenocarcinoma of the pancreas.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven adenocarcinoma of the pancreas and documented metastases. Patients must not be eligible for surgical treatment and must have adequate bone marrow, kidney, and liver function. Patients may not have received prior chemotherapy, have significant intrinsic heart disease, be older than 75 years, have a Karnofsky status of less than 60 percent, or have an active second type of tumor.

PROTOCOL OUTLINE: Randomized study. After stratification, patients are randomly assigned to Arm I or Arm II.

Arm I: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 3-Drug Combination Chemotherapy. ADR; BCNU, NSC-409962; Ftorafur, FT, NSC-148958.

STRATIFICATION BY: Participating institutions, measurable disease (nonmeasurable vs. measurable), prior radiation therapy (yes vs. no), status of primary tumor (resected vs. not resected), Karnofsky performance status (60-70 percent vs. 80-100 percent), weight loss within past 2 months (10 percent or less vs. more than 10 percent).

SPECIAL STUDY PARAMETERS: Tumor measurements and metastatic sites, Karnofsky performance status, bone and liver scans, chest x-ray, CAT scan, EKG, Echo, kidney and liver function tests, rectal examination.

END POINTS: Response/remission rate, duration of response, survival time, objective tumor response.

CURRENT STATUS: About 35 patients will be entered onto each arm. The study will require 2 years for patient entry and an additional year for follow-up.

DOSAGE SCHEDULE:

Arm I: ADR - 50 mg/sqm iv on day 1; 5-FU - 500 mg/sqm iv push on days 1, 2, and 3. Cycles repeated q 21 days for 2 years.

Arm II: BCNU - 100 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 1; FT - 2 g/sqm iv on days 1 and 2; all medications given by slow iv infusion. Cycles repeated q 28 days for 2 years.

Patients will be completely re-evaluated at the end of 2 years of treatment. Disease-free patients will then be taken off treatment, those with stable disease will be continued, and failures will go off study. When the total cumulative dose of ADR in either arm reaches 500 mg/sqm and the patient still has a significant clinical response, additional therapy will consist of BCNU - 150 mg/sqm iv on day 1 plus 5-FU - 325 mg/sqm iv push on days 1 through 5, courses repeating q 5 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules; BCNU - 100 mg vials; 5-FU - 500 mg ampules; FT - 0.5 and 2 g vials.

DATE SUMMARIZED: 07/80

2.0043 CONVENTIONAL RADIOTHERAPY PLUS 5-FU VS BRAGG PEAK HELIUM ION RADIOTHERAPY PLUS 5-FU FOR ALL STAGES OF PANCREATIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) NCOG-3P81; RTOG-7910

OBJECTIVES:

I. Compare effects of conventional radiotherapy plus chemotherapy with 5-fluorouracil (5-FU) vs. Bragg peak helium ion radiotherapy plus 5-FU for local and regional adenocarcinoma of the pancreas.

II. Determine differences in control rates based on anatomical stage of disease.

III. Compare tolerance to chemotherapy with 5-FU for patients treated with conventional radiotherapy to those treated with heavy particle radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients up to 75 years of age with histologically confirmed, any stage adenocarcinoma of pancreas who have reasonable expectation of completing protocol. Patients must have Karnofsky performance status of at least 60% and adequate liver, kidney and bone marrow function. Patients must not have had significant prior radiotherapy to pancreas, significant chemotherapy or potentially curative surgery (except bypass). They must not have metastases beyond the first relay nodes, or be pregnant.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus Single-agent Chemotherapy. At least 4 MeV x-ray to primary lesion and adjacent tissue; plus 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Radiotherapy plus Single-agent Chemotherapy. 230 MeV/amu charged particle beam of helium to primary lesion and adjacent tissue; plus 5-FU.

STRATIFICATION: Participating institutions; disease stage: T and N status, histology: G-1 vs. G-2 vs. G-3; tumor site within pancreas: head vs. body vs. tail vs. diffuse; surgical bypass: yes vs. no.

SPECIAL STUDY PARAMETERS: Exploratory laparotomy, needle biopsies of pancreas and liver, CAT scans, hematologic, liver and kidney function tests.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival, survival rate, quality of survival, disease-free interval.

CURRENT STATUS: 100 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: 5400 rad minimum (minimum rate 30 rad/min) in 5 fractions/week (maximum 33 fractions) in blocks of 2000 rads given over 2 weeks with a 2-week rest period between blocks to primary tumor; 4000 rads minimum in 5 fractions/week (maximum 22 fractions) to adjacent grossly uninvolved tissues and nodes; 5-FU - 500 mg/sqm iv push on days 1, 2 and 3 of each Radiotherapy block and 15 to 30 mg/k q week beginning 2 weeks after completion of Radiotherapy.

Arm II: External Helium Radiotherapy as in Arm I except 4 fractions/week with 5 to 10% incremental increases in dose after 10 patients if toxicity/morbidity allows; 5-FU, as in Arm I, except q 28 days and for a maximum of 2 cycles. Do not exceed 12 weeks of Radiotherapy. Continue Chemotherapy for 2 years, then discontinue if patients have no disease and continue if patients have static disease. Remove from study patients with disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

2.0044 NEUTRON THERAPY IN THE TREATMENT OF NONRESECTABLE ADENOCARCINOMA OF THE PANCREAS

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PROTOCOL NUMBER(S) RTOG-7921

OBJECTIVES:

I. Evaluate the effectiveness of high-energy neutron beams alone or in combination with low LET therapy in local control and alleviating symptoms of adenocarcinoma of the pancreas.

II. Evaluate the degree and duration of palliative relief attained.

III. Determine the time of onset, the evolution, and the severity of radiation injury in normal tissues.

IV. Estimate the time of local recurrence or of the appearance of metastases.

V. Determine survival rates at 1, 2, 3, and 5 years.

PROTOCOL ENTRY CRITERIA: Patients with nonresectable, histologically documented adenocarcinoma of the pancreas who are at least 10 days past major abdominal surgery and who have no evidence of distant metastases. Patients must have adequate bone marrow function and must not have had prior chemotherapy or radiotherapy. Patients must have disease of Stage T1-3, T4, or N plus and must be ambulatory and capable of outpatient treatment. Patients must not have chronic kidney disease, previous or concurrent cancer except skin cancer, intercurrent acute complications, or tumors requiring a target volume greater than 1700 cu cm. When possible, patients should have the upper, lower, and lateral margins of macroscopic disease marked by surgical clips at the time of laparotomy.

PROTOCOL OUTLINE: Randomized study. A facility may randomize patients into two or three arms, but all must choose the control photon arm.

Arm I: Radiotherapy. Photon treatment.

Arm II: Radiotherapy. Mixed-Beam treatment.

Arm III: Radiotherapy. Neutron treatment.

STRATIFICATION BY: Participating institutions; disease stage: T and N status; tumor site within the pancreas: head vs. body/tail vs. diffuse.

SPECIAL STUDY PARAMETERS: Liver function tests, kidney function tests, CT scan, CEA.

END POINTS: Survival time, quality of survival, tumor response, response of regional node metastases, time and site of distant metastasis, time and site of local recurrence, acute and late response of normal tissue, patient functional status during survival.

CURRENT STATUS: Between 30 and 75 patients will be required for each arm for statistical validity.

DOSAGE SCHEDULE:

Arm I: 6400 rad photon/electron in 6.5 to 7.5 weeks at 180 to 200 rad per fraction.

Arm II: 3800 rad in 19 fractions photon/electron plus 910 rad (Fermi) in 13 fractions neutron over 6.5 to 7.5 weeks.

Arm III: 2200 rad (Fermi) plus or minus 100 rad in 15 fractions, 2 fractions/week over 7 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 06/80

2.0045 PHASE II CHEMOTHERAPY WITH CHLOROZOTOCIN FOR SURGICALLY INCURABLE ISLET CELL CARCINOMA

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PROTOCOL NUMBER(S) SWOG-7935

OBJECTIVES:

I. Study the response of functioning and non-functioning islet cell carcinomas to chlorozotocin.

II. Review pathology materials on all patients entered into this study.

PROTOCOL ENTRY CRITERIA: Patients with symptomatic, measurable, biopsy-proven islet cell carcinoma not amenable to surgical therapy. Patients must have a minimum life expectancy of 6 weeks and adequate hematologic and renal status.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

STRATIFICATION: Participating institutions, prior streptozotocin therapy.

SPECIAL STUDY PARAMETERS: CAT and liver scans; serum gastrin, serum insulin, pancreatic polypeptide levels.

END POINTS: Objective tumor response, response/remission rate, relapse rate.

CURRENT STATUS: At least 15 patients will be entered.

DOSAGE SCHEDULE:

CLZ - 200 mg/sqm (poor-risk patients 65 years old or over, impaired bone marrow reserve, poor response to prior Chemotherapy start at 100 mg/sqm) iv on day 1. Repeat course q 6 weeks or when toxicity permits. Remove patients with progressive disease after first course.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLZ - 50 mg vials.

DATE SUMMARIZED: 02/80

2.0046 ADJUVANT CHEMOTHERAPY WITH 5-FLUOROURACIL AND RADIOTHERAPY FOLLOWING CURATIVE RESECTION FOR PANCREATIC ADENOCARCINOMA

Schein, P. S., (202-625-7081) Gastrointestinal Tumor Study Group, 850 Sligo Ave., Suite 601, Silver Spring, Maryland, 20910, United States of America

PROTOCOL NUMBER(S) GTSG-9173; MAYO-701883; SFCC-7458; SFCC-PANC-ONE

OBJECTIVES:

I. Determine whether postoperative adjuvant therapy with 5-fluorouracil and supervoltage irradiation can increase the disease-free interval and length of survival in patients with curable pancreatic adenocarcinoma of the ductal, acinar, and undifferentiated variety.

PROTOCOL ENTRY CRITERIA: Histologically confirmed acinar, ductal, or undifferentiated pancreatic adenocarcinoma. Enter patients who have undergone curative resection, with either Whipple procedure or total pancreatectomy, prior to entry. Patients who, due to vascular anastomosis, have undergone subtotal pancreatectomy with complete excision of recognizable disease are also eligible (Addendum #1).

PROTOCOL OUTLINE: Randomized study. Randomize patients 4 to 10 weeks following resection.

Arm I: Control patients. No further therapy.

Arm II: Radiotherapy plus Single-agent Chemotherapy. Supervoltage Radiotherapy plus 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Primary location: head or body and tail of pancreas; type of resection: Whipple procedure, total pancreatectomy; degree of differentiation: well, medium and undifferentiated; stage of disease: confined to pancreas, contiguous invasion or invasion of regional lymph nodes.

SPECIAL STUDY PARAMETERS: Liver scans; serum CEA; skin tests (DNCB and other recall antigens).

END POINTS: Duration of disease-free interval; duration of survival.

CURRENT STATUS: Approximately 10 patients per year to be entered for a minimum of 150 total patients.

DOSAGE SCHEDULE:

Arm I: No therapy.

Arm II: Radiotherapy (supervoltage). Two courses of 2000 rads per course given over 5 to 6 days per week with a 2-week rest interval between courses. 5-FU - 500 mg/sqm/day iv push x 3 days beginning on day 1 of each course of radiotherapy.

Maintenance: Enter patients who at completion of radiotherapy have adequate wbc's, platelets and hemoglobulin. 5-FU - 500 mg/sqm iv push once a week. Continue 5-FU until relapse or for 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

PATIENT ACCRUAL: 00331278

2.0047 SPLIT-COURSE RADIOTHERAPY PLUS 5-FLUOROURACIL VS CONTINUOUS RADIOTHERAPY PLUS ADRIAMYCIN FOR UNRESECTABLE PANCREATIC CARCINOMA

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PROTOCOL NUMBER(S) GTSG-9277

OBJECTIVES:

I. Compare split-course radiotherapy plus 5-fluorouracil to continuous radiotherapy plus adriamycin for locally unresectable nonmetastatic carcinoma of the pancreas.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven (surgical staging mandatory. Addendum 3, April 1980), locally unresectable adenocarcinoma of the pancreas only (ductal, acinar, or undifferentiated variety, including periampullary carcinoma presumed to be pancreatic in origin) with entire area of malignant disease encompassed in an area not to exceed 400 square centimeters on the anterior-posterior projection. Patients must have a performance level below 3, adequate oral nutrition, total bilirubin less than 3 mg%, and adequate hematologic function. Patients must not have had previous systemic cancer chemotherapy, or previous radiation in field of this study.

PROTOCOL OUTLINE: Randomized study. Randomize patients 3 to 6 weeks following surgery.

Arm I: Radiotherapy plus Single-agent Chemotherapy. Split-course supervoltage with linear accelerator to entire pancreas and pancreatic bed including areas of resected disease; plus 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Radiotherapy plus Single-agent Chemotherapy. Continuous supervoltage with linear accelerator to area described in Arm I; plus Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions; ECOG performance status: 0 vs. 1 vs. 2; location within pancreas of primary lesion: head vs. other; silver clip status: tumor marked vs. tumor not marked.

SPECIAL STUDY PARAMETERS: Kidney and liver function tests, 2-hour postprandial glucose or FBS, serum albumin, prothrombin time, skin tests for recall antigens, CEA, liver scan.

END POINTS: Length of survival, time to progression, toxicity/morbidity of treatment, response/remission rate, patterns of failure, pain relief.

CURRENT STATUS: 150 patients will be entered in 3 years.

DOSAGE SCHEDULE: Enter patients within 1 week after randomization.

Arm I: 2000 rads to entire pancreas and pancreatic bed including areas of resected disease for first 2 courses and only to known tumor-bearing area for the third course (all not exceeding 400 square centimeters) for a total of 3 courses separated by 2 weeks; 5-FU - 500 mg/sqm/day iv push on days 1 through 3 of each 2000 rad course of Radiotherapy, and q week for 2 years beginning 4 weeks after final course of Radiotherapy or until disease progression. Monitor wbc immediately prior to each of the first 4 weekly doses of 5-FU and q 2 weeks thereafter. Temporarily interrupt Chemotherapy if wbc falls below 4000. Monitor wbc twice weekly and hemoglobin and platelets weekly during Radiotherapy; and temporarily interrupt therapy when wbc falls below 2000 and platelets below 100,000.

Arm II: 4000 rads to area described in Arm I starting on a Monday or Tuesday (if started on a Wednesday, give a radiation dose on that Saturday); ADR - 15 mg/sqm iv within 1 hour preceeding initiation of Radiotherapy; 10 mg/sqm within 1 hour preceeding Radiotherapy q Monday thereafter and on the last day of Radiotherapy if it is a Friday, otherwise on the following Monday; then Maintenance on 60 mg/sqm q 3 weeks for 3 courses and q 4 weeks for 5 courses. Limit total dose to 540 mg/sqm. Four weeks after 8 courses of Maintenance, begin 5-FU - 500 mg/sqm iv q 7 days for 2 years or until disease progression. Do not administer ADR to patients with serum bilirubin greater than 3 mg%, and decrease starting Maintenance dose to 40 mg/sqm if serum bilirubin is greater than 1.5 mg%. Check wbc, hemoglobin, and platelet count twice weekly during Radiotherapy, and delay ADR if the wbc is less than 2000 (4000, Addendum 2, November 1978) or platelets less than 100,000. Postpone therapy while transfusing patients to obtain Hb level above 10 gms (Addendum 1, September 1978).

Dosage modifications according to nadir counts and for gastrointestinal or mucocutaneous toxicity are given (Addendum 1, September 1978).

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00211278

2.0048 PHASE II CHEMOTHERAPY WITH HMM, DAG, TGDR, ICRF-159, MTS, OR CLZ AND WITH SMF (5-FU/MITO/SZC) FOR ADVANCED CARCINOMA OF THE PANCREAS

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PROTOCOL NUMBER(S) GTSG-9376; MAYO-764301

OBJECTIVES:

I. Establish single-agent activity of beta-2'-deoxythioguanosine (TGDR), ICRF-159, dianhydrogalactitol (DAG), hexamethylmelamine (HMM), maytansine (MTS) and chlorozotocin (CLZ) (Revision, September 1977) for advanced measurable pancreatic cancer, using an established dose, route and schedule of administration for each drug.

II. Test the new drug combination SMF consisting of 5-fluorouracil (5-FU), mitomycin-C (MITO) and streptozotocin (SZC), which has undergone pilot studies at Georgetown University Hospital.

III. Determine the percentage of patients achieving objective response, complete or partial, and the duration of response while the patient is maintained on continuous therapy with any of the above regimens.

IV. Determine the relationship of response and its quality to ultimate patient survival.

PROTOCOL ENTRY CRITERIA: Patients with measurable lesions of adenocarcinoma of the pancreas of ductal, acinar or undifferentiated variety, not amenable to curative surgery or primary radiotherapy. Patients must have adequate bone marrow and renal function.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Dianhydrogalactitol, DAG, NSC-132313. (Arm terminated, May 1977).

Arm II: 3-Drug Combination Chemotherapy. Do not enter patients with abnormal renal function. SMF: weekly schedule. 5-Fluorouracil, 5-FU, NSC-19893; Mitomycin-C, MITO, NSC-26980; Streptozotocin, SZC, NSC-85998.

Arm III: 3-Drug Combination Chemotherapy, SMF: Loading course. 5-FU, MITO, SZC. (Arm terminated, February 1979).

Arm IV: Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

Arm V: Single-agent Chemotherapy. Beta-2'-deoxythioguanosine, TGDR, NSC-71261. (Arm terminated, Addendum 2, September 1977).

Arm VI: Single-agent Chemotherapy. ICRF-159, NSC-129943. (Arm terminated, Addendum 2, September 1977.)

Arm VII: Single-agent chemotherapy. Do not enter patients with abnormal liver function or prior vinca alkaloid therapy. Maytansine, MTS, NSC-153858.

Arm VIII: Single-agent Chemotherapy. Do not enter patients with abnormal renal function or with prior nitrosourea therapy. Chlorozotozin, CLZ, NSC-178248.

STRATIFICATION BY: Performance status, prior surgery, disease status, prior therapy, participating institutions.

SPECIAL STUDY PARAMETERS: CEA, chest X-ray, liver scan.

END POINTS: Toxicity/morbidity of treatment, survival rate, response/remission rate, objective tumor response, response duration, quality of survival.

CURRENT STATUS: 80 patients per year will be entered.

DOSAGE SCHEDULE:

Arm I: DAG - 25 mg/sqm/day iv push on days 1 through 5 and on days 36 through 40. Repeat course q 5 weeks.

Arm II: 5-FU - 600 mg/sqm iv on days 1, 8, 29 and 36. Repeat course beginning on day 57; SZC - 1 mg/sqm over 10 to 20 minutes on days 1, 8, 29 and 36 after the injection of 5-FU. Repeat course beginning on day 57; MITO - 10 mg/sqm q 8 weeks through a rapidly running iv. Monitor urinary function and wbc.

Arm III: 5-FU (when MITO is given) - 300 mg/sqm on days 1 through 5 q 10 weeks; 5-FU (when MITO is not given) - 350 mg/sqm q 10 weeks beginning on days 36-40; SZC - 350 mg/sqm on days 1 through 5 q 5 weeks; MITO - 10 mg/sqm iv on day 1. Repeat q 10 weeks. Monitor urinary function and wbc.

Arm IV: HMM - 320 mg/sqm po in 4 divided doses given after meals and at bedtime. Continue therapy until progression.

Arm V: TGDR - 100 mg/sqm iv on days 1 through 5. Repeat q 3 weeks.

Arm VI: ICRF-159 - 850 mg/sqm/day po in 3 divided doses given every 8 hours on days 1 through 3. Repeat therapy q 4 weeks.

Arm VII: MTS - 0.6 mg/sqm iv on day 1, 2 and 3 q 3 weeks for 3 courses. If patient is stable or responding, follow with maintenance course given q 4 weeks.

Arm VIII: CLZ - high dose, amount not given.

Continue therapy of each single agent at least 6 weeks, combination therapy for at least one cycle or 8 weeks. Rerandomize patients with disease progression after 6 or 8 weeks to one of the remaining eligible treatment Arms or follow up patient until off study. Continue same therapy on patients with objective response or stable disease. Follow all patients until death. According to revision September 1977 and Addendum 1, October 1978: Rerandomize patients exiting from Arms II and III to Arms VII or VIII, and cross over patients exiting from Arms IV, VII and VIII to Arm II.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DAG - 50 mg vials; 5-FU, SZC, and MITO - none given; HMM - 50 and 100 mg capsules; TGDR - 50 and 200 mg vials; ICRF-159 - 50, 250 and 500 mg tablets, MTS - 0.25 mg vials; CLZ - 50 mg vials.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 02021278

2.0049 PHASE II CHEMOTHERAPY FOR ADVANCED MEASURABLE PANCREATIC CARCINOMA-A MASTER PROTOCOL

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PROTOCOL NUMBER(S) GTSG-9376R

OBJECTIVES:

I. Estimate the level of effectiveness for the single agents and multiple drug combinations being evaluated in a selected mix of patients with advanced pancreatic cancer using the criterion of objective tumor response-partial or complete.

II. Determine the quality and duration of response and its relationship to survival.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable adenocarcinoma of the pancreas (ductal, acinar or undifferentiated, but excluding islet cell and cystadenocarcinoma). A primary lesion in the pancreas must be proven or strongly presumed on the basis of surgery, biopsy, and clinical findings. The disease must not be amenable to curative surgery or primary radiotherapeutic management. Prior abdominal surgery must have been performed at least 3 weeks prior to entry (2 weeks for abdominal exploration with biopsy only). Patients must be at least 1 month beyond prior radiotherapy or chemotherapy (7 weeks beyond any nitrosourea). Patients who have relapsed following primary surgery are eligible only in cases of disseminated disease. Patients who relapse or fail to respond to primary radiotherapy with or without 5-fluorouracil are ineligible for the SMF combination chemotherapy. Bone marrow function must be adequate.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. SMF: Streptozotocin, SCZ, NSC-85998; Mitomycin-C, MITO, NSC-26980; 5-Fluorouracil, 5-FU, NSC-19893. Upon progression, patients are rerandomized to Maytansine, MTS, NSC-153858 or Hexamethylmelamine, HMM, NSC-13875.

Arm II: Single-agent Chemotherapy plus 3-Drug Combination Chemotherapy. HMM; followed by SMF.

Arm III: Single-agent Chemotherapy plus 3-Drug Combination Chemotherapy. Dianhydrogalactitol, DAG, NSC-132313, followed by SMF.

Arm IV: Single-agent Chemotherapy plus 3-Drug Combination Chemotherapy. MTS; followed by SMF.

Arm V: 3-Drug Combination Chemotherapy. SMF. Upon progression, patients are rerandomized to MTS or HMM. (Patient entry onto this arm has been terminated, Addendum 1, March 1980.)

Arm VI: Single-agent Chemotherapy plus 3-Drug Combination Chemotherapy. Chlorozotocin, CLZ, NSC-178248 (low dose); followed by SMF.

Arm VII: Single-agent Chemotherapy plus 3-Drug Combination Chemotherapy. CLZ (high dose); followed by SMF.

Arm VIII: 3-Drug Combination Chemotherapy. FAM: 5-FU; Adriamycin, ADR, NSC-123127; MITO. Upon progression, MTS or HMM.

STRATIFICATION BY: ECOG performance status: 0 or 1, no prior chemotherapy vs. 0 or 1, prior chemotherapy vs. 2; major surgery: yes vs. no; creatinine: 1.5 mg percent or more; bilirubin: 1.7 mg percent or more; heart disease: yes vs. no; prior radiotherapy and/or chemotherapy with 5-FU, nitrosourea, ADR or MITO, vinca alkaloids: yes vs. no.

SPECIAL STUDY PARAMETERS: Fasting blood glucose, prothrombin time, serum total protein and albumin, chest x-ray, immunology and skin tests, CEA, liver scan (optional).

END POINTS: Length of survival, objective tumor response, response/remission rate.

CURRENT STATUS: 80 patients (10/arm) will be accrued over a 36-month period.

DOSAGE SCHEDULE:

Arm I: SMF (weekly intermittent schedule): 5-FU - 600 mg/sqm iv on days 1, 8, 29, and 36; SCZ - 1 g/sqm iv on days 1, 8, 29, and 36 after 5-FU; MITO - 10 mg/sqm iv q 8 weeks. Repeat course beginning on day 57. Patients with rapidly progressing disease at 8 weeks are rerandomized: MTS - 0.6 mg/sqm/day iv rapid push on days 1, 2, and 3, repeating q 3 weeks for 3 courses, then Maintenance therapy q 4 weeks; or HMM - 320 mg/sqm in 4 divided doses po daily until progression or for at least 6 weeks.

Arm II: HMM - 320 mg/sqm/day in 4 divided doses daily for 6 weeks. 5-FU, SCZ, and MITO as in Arm I.

Arm III: DAG - 25 mg/sqm/day iv rapid push on days 1 through 5. Repeat on days 36 through 40; plus 5-FU, SCZ, and MITO as in Arm I.

Arm IV: MTS - 0.6 mg/sqm/day iv rapid push on days 1, 2, and 3. Repeat q 3 weeks for 3 courses. Give 5-FU, SCZ, and MITO as in Arm I.

Arm V: SMF (loading course): 5-FU - 300 mg/sqm iv on days 1 through 5, 71 through 75, 141 through 145, etc., repeating at 5-week intervals; SCZ - 350 mg/sqm iv for 5 days, repeating at 5-week intervals; MITO - 10 mg/sqm iv q 10 weeks, starting on day 1. Rerandomize to MTS or HMM as in Arm I. (This arm closed to patient entry, Addendum 1, March 1980.)

Arm VI: CLZ - 120 mg/sqm rapid iv q 6 weeks. 5-FU, SCZ, and MITO as in Arm I.

Arm VII: CLZ - 175 mg/sqm rapid iv q 6 weeks. 5-FU, SCZ, and MITO as in Arm I.

Arm VIII: FAM: 5-FU - 600 mg/sqm iv rapid push on days 1, 8, 29, and 36; ADR - 30 mg/sqm iv over 5 minutes on days 1 and 29, total dose not to exceed 500 mg/sqm; MITO - 10 mg/sqm iv bolus q 8 weeks. Repeat cycle every 8 weeks (56 days) until progression of disease, then rerandomize to MTS or HMM as in Arm I.

All patients will be followed until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: HMM - 50 and 100 mg capsules; DAG - 50 mg vials; MTS - 0.25 mg vials; CLZ - 50 mg vials; 5-FU - ADR, MITO, and SCZ - not given.

DATE SUMMARIZED: 10/80

2.0050 HEAVY CHARGED PARTICLE RADIATION THERAPY FOR CARCINOMA OF THE PANCREAS

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PROTOCOL NUMBER(S) VASOG-LBL-PAN-1; VASOG-7901P

OBJECTIVES:

I. Evaluate the effectiveness of Bragg peak heavy charged particle radiation therapy in the treatment of local and regional carcinoma of the pancreas.

II. Define differences in control rates based on anatomical stage of disease.

III. Compare the radiation toxicity using conventional techniques as compared with heavy charged particle techniques.

PROTOCOL ENTRY CRITERIA: Patients with T1-4, N0-2, M0 biopsy-proven carcinoma of the pancreas. Patients must be under 75 years of age and have a Karnofsky performance status of at least 50 percent; hepatic, renal, hematologic, and bone marrow function must be adequate. Patients must not have liver metastasis, metastases below the first station nodes, significant prior radiotherapy to the pancreas, active uncontrollable infection or evidence of a second malignancy other than skin cancer. Patients must not be pregnant.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Heavy charged particle beams of carbon or neon accelerated at the Bevalac.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements; CT scan; hematologic, renal, and hepatic function tests; EKG; upper GI; endoscopy; liver scan; chest x-ray; rectal examination.

END POINTS: Control of disease, disease-free interval, length and quality of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Heavy charged particle beam - 6000 Co-60 gamma ray rad equivalents (CoRE) to the primary lesion and adjacent lymph nodes in 200-225 CoRE fractions in 7.5 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 10/80

2.0051 RADIOTHERAPY WITH OR WITHOUT 5-FLUOROURACIL CHEMOTHERAPY FOR UNRESECTABLE PANCREATIC CARCINOMA

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PROTOCOL NUMBER(S) ARG-LACRIP-8

OBJECTIVES: This protocol is being done in cooperation with Georgetown University.

I. Compare the activity of 5-fluorouracil plus radiation vs. radiotherapy alone for locally unresectable pancreatic carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed pancreatic adenocarcinoma of ductal, acinar or undifferentiated types, including islet cell or cystadenocarcinoma, carcinoid tumors, and duodenal or ampullary carcinomas. Patients must have locally unresectable disease not over 400 square cm in area and confined to the pancreas, regional lymph nodes and peritoneum. Patients must have completed previous chemotherapy at least one year prior to entry and must not have had radiotherapy to the field under treatment. Patients must have adequate oral nutrition and stable weight for 2 weeks prior to entry. Patients must not have significant coexistent disease and must have adequate hepatic, renal and bone marrow function.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Supervoltage.

Arm II: Single-agent Chemotherapy plus Radiotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Location of primary lesion: head vs. body and/or tail; degree of differentiation: Broders grade I vs. Broders grades II and III vs. Broders grade IV; prior surgery: partial resection plus bypass vs. biopsy plus bypass vs. biopsy vs. criteria for unresectability undefined.

SPECIAL STUDY PARAMETERS: Hepatic, renal, bone marrow function; CEA; serum glucose; liver scan.

END POINTS: Length of survival, duration of response, toxicity/moribidity of treatment.

CURRENT STATUS: 20 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: 2000 rads in 2 weeks to the entire pancreas and unresected tumor. Repeat course after 2 weeks rest.

Arm II: 5-FU - 500 mg/sqm iv on days 1 through 3 plus Radiotherapy as in Arm I on days 1 through 14. Repeat course with 5-FU, Radiotherapy beginning on day 29.

Maintenance: Start 4 weeks after completion of last course of Radiotherapy. 5-FU - 500 mg/sqm iv on day 1. Repeat q week for 2 years or until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/78

2.0052 5-FU PLUS RADIOTHERAPY VS SMF (SZC/MITO/5-FU) FOR LOCALLY UNRESECTABLE CARCINOMA OF THE PANCREAS

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Compos 726, 1426 Buenos Aires, Argentina
PROTOCOL NUMBER(S) ARG-PAN-7705

OBJECTIVES:

I. Compare 5-fluorouracil (5-FU) plus radiation in locally unresectable pancreatic carcinoma against the combination of streptozotocin (SZC)/mitomycin (MITO)/5-FU.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed ductal, acinar or undifferentiated adenocarcinoma of pancreas, including islet cell, cystadeno, ampullary and duodenal carcinomas and carcinoid tumors. Patients must have unresectable disease confined within an area of 400 sqm to the pancreas, regional lymph nodes and peritoneum. Patients must have had no prior Radiotherapy to the area under treatment, no systemic Chemotherapy for 1 year prior to entry and must have adequate oral nutrition and bone marrow function.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy plus Radiotherapy. 5-Fluorouracil, 5-FU, NSC-19893; plus supervoltage irradiation.

Arm II: 3-Drug Combination Chemotherapy. SMF: Streptozotocin, SZC, NSC-85998; Mitomycin-C, MITO, NSC-26980; 5-FU.

STRATIFICATION BY: Participating institutions; location of primary lesion: head vs. body and/or tail; degree of differentiation: well vs. medium vs. undifferentiated; prior surgery: partial resection/bypass vs. biopsy/bypass vs. biopsy vs. undefined unresectability.

SPECIAL STUDY PARAMETERS: CEA, liver scan.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE: Enter patients within 3 to 6 weeks following surgery.

Arm I: 2000 rad in 2 weeks to unresected tumor and entire pancreas. Repeat course once after a 2-week rest. 5-FU - 500 mg/sqm iv on days 1 through 3 of each course of Radiotherapy. 4 weeks after the end of Radiotherapy, begin 500 mg/sqm iv q 7 days for 2 years or until disease progresses.

Arm II: 5-FU - 600 mg/sqm iv on days 1, 8, 29 and 36; SZC - 1 gm/sqm iv on days 1, 8, 29 and 36 after 5-FU; MITO - 10 mg/sqm iv on day 1. Repeat course q 8 weeks.

Remove patients from study when disease progresses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/78

2D. HEPATOBILIARY

2.0053 PHASE II-III TRIAL OF NEOCARZINOSTATIN VS M-AMSA OR ADR IN ADVANCED HEPATOCELLULAR CARCINOMA

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PROTOCOL NUMBER(S) EST-1280

OBJECTIVES:

I. Compare neocarzinostatin and m-AMSA in a Phase II study in American patients with advanced liver cancer.

II. Compare neocarzinostatin and adriamycin in a Phase III trial in South African patients with advanced liver cancer.

III. Correlate histological differentiation in primary hepatocellular cancer with prognosis and response, and evaluate the effect of concomitant liver disease such as cirrhosis, siderosis, or chronic Budd Chiari disease.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed metastatic, residual, or recurrent hepatocellular carcinoma with a measurable area of disease. Patients must be at least 3 weeks beyond major surgery and at least 2 weeks after exploration. Patients may not have received chemotherapy or radiotherapy within the previous month and must be free of severe malnutrition and active infectious processes. Hematological and renal parameters must be adequate and the performance status must be less than 4. There must be no portal systemic encephalopathy, varices with recent hemorrhage, or active heart disease. A prothrombin time of greater than 50 percent must be responsive to Vitamin K.

PROTOCOL OUTLINE: Randomized study.

Enter American and South African patients to Arm I, American patients only to Arm II, and South African patients only to Arm III.

Arm I: Single-agent Chemotherapy. Neocarzinostatin, NCS, NSC-157365.

Arm II: Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

Arm III: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Nationality, participating institutions, performance status (0 vs. 1 vs. 2 vs. 3), cirrhosis (yes vs. no), jaundice (yes vs. no).

SPECIAL STUDY PARAMETERS: Hematologic parameters, kidney and liver function tests, serum protein electrophoreses, prothrombin time, HAA/HBS/AG, alpha-fetoprotein.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: About 35 patients will have been entered in the two American Arms in 1.5 years and about 20 patients in each of the South African Arms.

DOSAGE SCHEDULE:

Arm I: NCS - 2250 units/sqm iv infusion on days 1 through 5, repeated q 28 days. Continue treatment as long as disease is stable or there is objective regression. In cases of objective progression or relapse after regression, American patients may be crossed over to Arm II and South African patients to Arm III.

Arm II: AMSA - 120 mg/sqm iv infusion q 3 weeks. Continue treatment as long as disease is stable or there is objective regression. In cases of objective progression or relapse after response, patients may be crossed over to Arm I.

Arm III: ADR - 60 mg/sqm rapid iv push on days 1, 22, and 43 and thereafter q 28 days to a maximum cumulative dose of 500 mg/sqm. Icteric patients and those with SGOT levels more than twice normal should receive only 40 mg/sqm. Patients will be re-evaluated on day 43. Continue treatment as long as disease is stable or there is evidence of CR or PR. In cases of progressive disease or relapse, patients may be crossed over to Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: NCS - 2000 unit ampules; AMSA - 75 mg vials; ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 07/80

2.0054 PHASE I-II PILOT CHEMOTHERAPY WITH INTRAHEPATIC ADR/5-FU PLUS RADIOTHERAPY FOR UNRESECTABLE PRIMARY OR METASTATIC LIVER CANCER

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PROTOCOL NUMBER(S) NCOG-P-3L71

OBJECTIVES:

I. Combine external irradiation of the liver with concomitant intrahepatic infusion of adriamycin (ADR) and 5-fluorouracil (5-FU) in order to assess the toxicity, response, and therefore, the efficacy of this modality of therapy.

PROTOCOL ENTRY CRITERIA: Patients with measurable histologically confirmed cancer of any origin metastatic to the liver, or patients with unresectable hepatocellular carcinoma. Patients must be between 16 and 75 years old, with a Karnofsky performance status of at least 40%, must have normal hematologic, cardiac, and renal function, and must not have had prior intrahepatic infusion therapy or maximal ADR chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study. 2-Drug Combination Chemotherapy plus Radiotherapy. Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893; plus Radiotherapy with megavoltage of Co-60 energy or higher.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Liver scan, liver measurements, CEA or AFP levels, IVP, SMA-12.

END POINTS: Response/remission rate, objective tumor response, survival time, response duration.

CURRENT STATUS: 5 to 30 patients will be entered in 7 to 9 months.

DOSAGE SCHEDULE:

5-FU - 10 mg/kg/day continuous intrahepatic artery infusion for a minimum of 6 days during Radiotherapy; ADR - 5 mg/sqm/day by intrahepatic artery bolus 2 hours prior to Radiotherapy. Stop 5-FU administration when ADR is given, then resume 5-FU infusion. Continue Chemotherapy until completion of Radiotherapy. Begin Radiotherapy 2 hours after ADR therapy. 2100 rad given in 7 fractions of 300 rad each over 6 to 8 days to entire liver, plus boost up to 5000 rad given at the discretion of the radiotherapist.

Appropriate systemic Chemotherapy may follow above treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; ADR - 10 mg ampules.

DATE SUMMARIZED: 05/79

2.0055 PHASE I-II RADIOTHERAPY AND INTRAHEPATIC ADR, 5-FU, MTX CHEMOTHERAPY FOR UNRESECTABLE METASTATIC OR PRIMARY LIVER CANCER

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PROTOCOL NUMBER(S) NCOG-P-3L81

OBJECTIVES:

I. Ascertain objective response rate of external radiotherapy plus combination intrahepatic artery (ih) chemotherapy with adriamycin (ADR), 5-fluorouracil (5-FU), methotrexate (MTX), and citrovorum factor (CF) rescue.

II. Measure duration of response and survival from date of onset of therapy and note progression of disease in areas other than liver.

III. Document the toxicities of this therapy.

PROTOCOL ENTRY CRITERIA: Patients 16 and 75 years old, with histologically confirmed cancer of any origin except bone marrow or lymph node with measurable metastatic liver disease or unresectable hepatocellular carcinoma. Patients must have had no prior liver or abdominal irradiation, no previous intrahepatic infusions with chemotherapy nor received the maximum tolerable dose of adriamycin nor have ascites or pleural effusion that would prohibit use of methotrexate or make hydration hazardous. Patients must have adequate hematological and renal function, Karnofsky status of at least 50% and have a minimum expected survival of 6 weeks. They must have an adequate cardiac status, prothrombin time below 15, and a BUN below 30 mg/%.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy plus 4-Drug Combination Intrahepatic Chemotherapy. 2 MeV Cobalt-60 up to 15 MeV maximum, plus Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: SMA-12, AFP, CEA, liver scan, CAT scan of liver, IVP, liver measurements.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, duration of response, length of survival, objective tumor response.

CURRENT STATUS: 25 patients will be entered in 6 to 7 months.

DOSAGE SCHEDULE:

Radiotherapy. 2100 rad given in 7 daily doses of 300 rad each to the entire liver, plus boost of 5000 rad to residual masses in the liver given at radiotherapist's discretion. Boost must not include more than 40% of the liver and must avoid other vital organs. Chemotherapy begins 2 hours prior to Radiotherapy. ADR - 5 mg/sqm/day (3 mg/sqm/day for patients with any prior chemotherapy) ih administered only on days when Radiotherapy is given: MTX - 240 mg/sqm ih on day 1 only immediately following first Radiotherapy treatment and urine alkalization and hydration, giving 150 mg/sqm in 20 min, then 90 mg/sqm in over 3 hours with heparin; 5-FU - 10 mg/kg/day ih as a continuous 24-hour infusion beginning as soon as MTX infusion is completed and continuing until end of Radiotherapy with interruption only for ADR dosages; CF - 25 mg/sqm given po, im or iv q 6 hours for 3 days beginning 24 hours after completion of MTX infusion. Continue Chemotherapy until end of radiation treatment. This may be followed by appropriate systemic Chemotherapy upon sufficent bone marrow recovery.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; ADR - 10 mg ampules; MTX - 50 mg vials; CF - 3 and 50 mg ampules.

DATE SUMMARIZED: 06/79

2.0056 PHASE III RADIOTHERAPY VS RADIOTHERAPY PLUS INTRAVENOUS OR INTRAHEPATIC INFUSION CHEMOTHERAPY WITH ADR/5-FU/MITO FOR LIVER CANCER

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PROTOCOL NUMBER(S) NCOG-3L91

OBJECTIVES:

I. Determine effect of radiotherapy vs. radiotherapy with intravenous or with intrahepatic infusion combination chemotherapy with adriamycin (ADR)/5-fluorouracil (5-FU)/mitomycin-C (MITO) for unresectable, hepatocellular carcinoma or metastases to the liver.

PROTOCOL ENTRY CRITERIA: Patients between 16 and 75 years of age with unresectable hepatocellular carcinoma or histologically-confirmed cancer of any origin (except lymph node or bone marrow) with measurable metastatic disease to liver. Patients must have Karnofsky performance status of at least 50, normal liver and kidney function, and adequate hematologic function. Patients must not have gross ascites or previous intrahepatic chemotherapy infusion.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Megavolt or Co-60 irradiation of entire liver.

Arm II: Radiotherapy plus Intravenous 3-Drug Combination Chemotherapy. Radiotherapy as in Arm I, plus FAM: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980.

Arm III: Radiotherapy plus Intrahepatic 3-Drug Combination Chemotherapy. Radiotherapy as in Arm I, plus FAM as in Arm II.

STRATIFICATION BY: Participating institutions; source of disease: hepatocellular vs. metastatic; Karnofsky performance status: 50-70 vs. 80-100; prior chemotherapy: yes vs. no; bilirubin: up to 2 vs. over 2.

SPECIAL STUDY PARAMETERS: Size, measurement, and scan (or CAT) of liver; intravenous pyelogram; Karnofsky performance status; liver, kidney, hematologic, and bone function; prothrombin and partial thromboplastin times; carcinoembryonic antigen and alpha fetoprotein.

END POINTS: Response/remission rate, duration of response, disease-free interval, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 180 to 200 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: 2100 rads in 7 fractions over 6 to 8 days.

Arm II: Radiotherapy as in Arm I; FAM: 5-FU - 10 mg/kg in 1000 cc D5W or normal saline iv over 24 hours on days 1 through 7; ADR - 3 mg/sqm (2 mg/sqm and 1 mg/sqm for patients with bilirubin greater than 1.5 and 3.0, respectively) iv slow push 2 hours prior to irradiation on days when Radiotherapy only is given (discontinue 5-FU during ADR); MITO - 18 mg/sqm iv over 2 to 3 minutes on day 1.

Arm III: Radiotherapy and FAM as in Arm II except: use catheter placed in hepatic artery, add 4000 units of Heparin to 5-FU solution, and infuse MITO over 30 to 45 minutes.

Continue therapy until completion of Radiotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: 5-FU - 10 mg ampules; ADR - 10 mg ampules; MITO - 5 mg vials.

DATE SUMMARIZED: 02/80

2.0057 PHASE I-II STUDY OF COMBINED MODALITY TREATMENT OF PRIMARY LIVER CANCER WITH ISOTOPIC IMMUNOGLOBULIN, LIVER IRRADIATION, AND ADR/5-FU

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PROTOCOL NUMBER(S) RTOG-7928

OBJECTIVES:

I. Determine the therapeutic efficacy of combining administration of radiolabeled anti-CEA or anti-ferritin with whole liver radiotherapy plus combination chemotherapy using adriamycin/5-fluorouracil in patients with primary liver cancer.

II. Determine the maximal tolerated dose of radiolabeled antibody and the toxicities associated with this treatment.

III. Determine the dose distributions of anti-CEA and anti-ferritin in the tumor and in the entire body and compare the dose distributions of the 2 antibodies in hepatoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented primary hepatic malignancy who have measurable or evaluable disease. Patients must have a Karnofsky performance status of greater than 30 upon entry and of greater than 60 prior to the immunoglobulin therapy. Bone marrow, hepatic, renal, cardiac, and pulmonary functions must be adequate. Patients must be less than 75 years of age and be cleared of active infection. They may have received no chemotherapy, surgery, or large field radiotherapy within 28 days prior to entry, and there may be no history of asthma or eczema.

PROTOCOL OUTLINE: Nonrandomized study. Following treatment on Regimens A and B, patients with hepatic biliary carcinoma are entered to Arm I and patients with hepatoma to Arm I or Arm II.

Regimen A: 2-Drug Combination Chemotherapy plus Radiotherapy. Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893; plus whole liver radiotherapy with either Cobalt-60 teletherapy or supervoltage energy equipment (at least 2 MeV).

Regimen B: 2-Drug Combination Chemotherapy. ADR; 5-FU.

Arm I: Isotopic Therapy. I-131-labeled anti-CEA.

Arm II: Isotopic Therapy. I-131-labeled anti-ferritin.

Maintenance (Revision August 1980): 2-Drug Combination Chemotherapy. ADR; 5-FU.

STRATIFICATION BY: Participating institutions, site of primary tumor (hepatoma vs. hepatic biliary).

SPECIAL STUDY PARAMETERS: Performance status, tumor measurements, hematologic parameters, electrolytes, liver and kidney function tests, chest x-ray, EKG, pulmonary function studies, CEA, ferritin, alpha fetoprotein, T3-T4, CAT scan, radioactivity counts.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment, objective tumor response.

DOSAGE SCHEDULE:

Regimen A: 2100 rad delivered to the entire liver through opposing AP/PA fields in 7 fractions of 300 rad each on days 1, 2, 4, 5, 8, 9, and 10; ADR - 15 mg iv 2 hours prior to Radiotherapy on days 1, 4, 8, and 10; 5-FU - 500 mg iv 2 hours prior to Radiotherapy on days 1, 4, 8, and 10.

Regimen B: ADR - 50 mg/sqm iv; 5-FU - 600 mg/sqm iv. Administer 1 month after liver irradiation and repeat after 28 days for a total of 2 cycles.

Arm I: I-131-labeled anti-CEA - initial dose 100 mCi. Escalation by 50 mCi over the previous dose in groups of 3 patients of each tumor type until the maximum tolerance dose is reached (not to exceed 200 mCi). At least 4 weeks of observation of treated patients will have passed before dose escalation begins in the next group of patients.

Arm II: I-131-labeled anti-ferritin - initial dose and escalation procedures as for anti-CEA in Arm I.

Maintenance (Revision August 1980): Two months after therapy in Arm I or Arm II, patients who had CR, PR, or SD after 2 cycles in Regimen B will receive monthly therapy with ADR - 50 mg/sqm iv; plus 5-FU - 600 mg/sqm iv until progression, at which time they will be taken off study. Those who had progressed after Regimen B will only be observed until progression after Arm I or Arm II.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; 5-FU - 500 mg vials.

DATE SUMMARIZED: 12/80

2.0058 PHASE II CHEMOTHERAPY WITH ADR/BLEO FOR PRIMARY LIVER, GALLBLADDER, AND BILE DUCT CARCINOMA

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PROTOCOL NUMBER(S) SEG-77GI0302; SEG-77GI223

OBJECTIVES:

I. Evaluate effectiveness and toxicity of chemotherapy with adriamycin/bleomycin for hepatocellular and cholangiocellular carcinoma of the gall bladder, or bile duct adenocarcinoma. (Protocol closed to hepatocellular carcinoma in 1980.)

PROTOCOL ENTRY CRITERIA: Patients with residual, recurrent or metastatic lesions of nonresectable, measurable hepatocellular (closed to hepatocellular in 1980), cholangiocellular, gallbladder or bile duct adenocarcinoma. Patients may not have had surgery in the previous three weeks, chemotherapy or radiation therapy in preceding four weeks, or exploration and biopsy in preceding two weeks.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Bleomycin, BLEO, NSC-125066.

STRATIFICATION BY: Participating institutions, tumor category, Karnofsky performance status, presence or absence of cirrhosis.

SPECIAL STUDY PARAMETERS: SMA-12, T-tube cholangiogram, liver and bone scan, CEA, alpha-feto protein.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, response/remission rate, response duration, survival rate.

CURRENT STATUS: About 50 patients are to be entered in two years.

DOSAGE SCHEDULE:

ADR - 60 mg/sqm (maximum total dose 600 mg/sqm) iv q 3 weeks concurrent with BLEO for a maximum of ten 21-day courses; BLEO - 10 mg/sqm/day (maximum total dose 300 mg) iv on days 1 and 4 q 7 days for 3 weeks for a maximum of five 21-day courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; BLEO - 15 unit vials.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00081078

2.0059 PHASE II CHEMOTHERAPY WITH AMSA FOR HEPATOCELLULAR, GALLBLADDER AND BILE DUCT CARCINOMA

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PROTOCOL NUMBER(S) SWOG-7920

OBJECTIVES:

I. Determine the efficacy of AMSA at a dose of 120 mg/sqm iv every three weeks in producing regressions or remissions in patients with hepatocellular, bile duct, and gallbladder carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with measurable and histologically confirmed, surgically incurable, residual, recurrent or metastatic hepatocellular, bile duct or gallbladder carcinoma. Patients must have a life expectancy of 4 weeks or more.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. AMSA, NSC-249992.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Liver function tests: SGOT, LDH, alkaline phosphatase; kidney function tests: BUN, creatinine; liver scan; CAT scan or ultrasound.

END POINTS: Response/remission rate, duration of response, objective tumor response.

CURRENT STATUS: 15 to 25 patients with hepatoma plus 15 patients each with gallbladder and biliary tract carcinoma will be entered in 1.5 years.

DOSAGE SCHEDULE:

AMSA - 150 mg/sqm (90 mg/sqm for poor-risk patients more than 65 years of age, prior abdominal or pelvic radiation, prior severe myelosuppression with chemotherapy, or bilirubin between 1.2 and 3.0 and 60 mg/sqm for patients with abnormal liver function, with bilirubin 3.0 or more, and with SGOT more than 3 times normal) iv in 500 ml dextrose water infusion over 1 hour given q 3 to 4 weeks if adequate hematologic and liver function.

Give at least two courses of treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 11/79

2.0060 PHASE II/PILOT INDUCTION WITH FUDR/ADR/SZC BY HEPATIC ARTERY INFUSION AND ADR/SZC/5-FU MAINTENANCE FOR NONRESECTABLE HEPATOMA

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PROTOCOL NUMBER(S) SWOG-7969

OBJECTIVES:

I. Determine the remission rate seen after Induction with intra-arterially infused floxuridine (FUDR)/adriamycin (ADR)/streptozotocin (SZC) in patients with hepatocellular carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, nonresectable, hepatocellular carcinoma localized to the liver. Patients must have adequate cardiac and renal status and no prior radio- or chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 3-Drug Combination Chemotherapy. Floxuridine, FUDR, NSC-27640; Adriamycin, ADR, NSC-123127; Streptozotocin, SZC, NSC-85998.

Maintenance: 3-Drug Combination Chemotherapy. ADR; SZC; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: CEA, alpha fetoprotein, liver scan, hepatic angiogram.

END POINTS: Objective tumor response.

CURRENT STATUS: 15 to 25 patients to be entered.

DOSAGE SCHEDULE:

Induction: ADR - 40 mg/sqm (start poor risk patients at 30 mg/sqm; maximum cumulative dose 500 mg/sqm) hepatic arterial infusion on day 1; FUDR - 50 mg/sqm (start poor risk patients at 40 mg/sqm) continuous hepatic arterial infusion on days 1 through 4; SZC - 300 mg/sqm hepatic arterial infusion on days 1 through 4. Repeat q 28 days for 2 courses. Enter responders to Maintenance.

Maintenance: 5-FU - 600 mg/sqm (start poor risk patients at 500 mg/sqm) iv on days 1 and 8; ADR - 40 mg/sqm (start poor risk patients at 30 mg/sqm) iv on day 1; SZC - 300 mg/sqm iv on days 1 through 4. Repeat q 4 weeks, omitting ADR when maximum dose is reached.

Enter patients with progressive disease after Maintenance Therapy to another course of Induction. Continue Induction if patient responds, repeating course q 28 days. Follow all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; SZC - 1 g ampules; FUDR - 500 mg containers; 5-FU - 500 mg ampules.

DATE SUMMARIZED: 02/80

2.0061 CHEMOTHERAPY WITH VP-16213 PLUS NEOCARZINOSTATIN FOR ADULT HEPATOCELLULAR CARCINOMA

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PROTOCOL NUMBER(S) BCRP-7809

OBJECTIVES:

I. Determine the therapeutic efficacy of neocarzinostatin plus VP-16213 in patients with hepatocellular carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven hepatocellular carcinoma that is not amenable to surgery. Patients must have measurable disease and be between the ages of 15 and 70 years.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. VP-16213, VP-16, NSC-141540; Neocarzinostatin, NCS, NSC-157365.

STRATIFICATION BY: Prognostic risk, age (over 50 vs. under 50), duration of symptoms (more or less than 3 months), weight loss (more or less than 15 percent), ascites (present vs. absent), cirrhosis (present vs. absent), degree of bilirubinemia (more or less than 2 micrograms/l).

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver function studies, tumor measurements, appropriate scans and x-rays, HAA, alpha-fetoprotein, CEA.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

VP-16 - 100 mg/sqm/day po for 5 days; NCS - 1000 U/sqm/day for 5 days in a 2-hour iv infusion. Repeat courses q 28 days. Continue treatment until unacceptable toxicity develops or until tumor progression after 3 courses of treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

2.0062 CHEMOTHERAPY WITH ADR/BCNU/5-FU WITH AND WITHOUT IMMUNOTHERAPY WITH C.PARVUM IN INOPERABLE PRIMARY AND METASTATIC CARCINOMA OF THE LIVER

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PROTOCOL NUMBER(S) RPMI-PPC-539

OBJECTIVES:

I. Compare the effect of 3-drug chemotherapy with adriamycin (ADR), BCNU and 5-fluorouracil (5-FU) vs. chemotherapy plus immunotherapy with intrahepatic Corynebacterium parvum (C.parvum) on remission duration and survival of patients with inoperable primary and metastatic carcinoma in the liver.

II. Determine the difference in response rate and toxicity of chemotherapy with and without immunotherapy.

PROTOCOL ENTRY CRITERIA: Patients with nonresectable primary and metastatic carcinoma of the liver. Patients must not be jaundiced and must have a creatinine less than 1.5 and acceptable hematologic parameters.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; BCNU, NSC-409962; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 3-Drug Chemotherapy plus Immunotherapy. ADR; BCNU; 5-FU; plus Corynebacterium parvum Burroughs-Wellcome, C.parvum B.W., NSC-220537.

STRATIFICATION BY: Primary vs. metastatic tumors.

SPECIAL STUDY PARAMETERS: AFP for patients with hepatoma; CEA for patients with metastatic disease.

END POINTS: Remission duration and survival.

CURRENT STATUS: 5 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: Courses of ADR, BCNU and 5-FU are administered at 6-week intervals; drug dosages are not specified.

Arm II: Chemotherapy as in Arm I, plus intrahepatic C.parvum B.W. on day 21 or 22 of each 6-week cycle.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 05/80

PATIENT ACCRUAL: 00050028

2.0063 PHASE II CHEMOTHERAPY WITH VP-16 FOR HEPATOCELLULAR CARCINOMA

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PROTOCOL NUMBER(S) EORTC-16784

OBJECTIVES:

I. Investigate the activity of VP-16 in hepatocellular cancer.

II. Determine the possible influence of the clinical staging in correlation to the therapeutic response.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven and measurable hepatocellular carcinoma with or without metastases. Patients must have no previous diagnosis of other tumor types and must have a Karnofsky index of more than 40.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. VP-16, NSC-141540.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Liver function tests, alphafetoprotein, liver scan, hepato-arteriogram, liver measurements, liver biopsy.

END POINTS: Response/remission rate; objective tumor response; toxicity/morbidity of treatment.

CURRENT STATUS: 14 to 25 patients will be entered.

DOSAGE SCHEDULE:

VP-16 - 120 mg/sqm po on days 1 through 5. Repeat course every 3 weeks for at least 2 courses or until disease progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/79

2E. COLON AND RECTUM

2.0064 PHASE II CHEMOTHERAPY WITH SPIROGERMANIUM FOR UNRESECTABLE, RECURRENT, OR METASTATIC COLORECTAL CARCINOMA

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PROTOCOL NUMBER(S) CLB-8075

OBJECTIVES:

I. Determine whether iv spirogermanium has any significant activity against advanced unresectable or metastatic adenocarcinoma of the colon or rectum.

PROTOCOL ENTRY CRITERIA: Patients with measurable and histologically confirmed unresectable or metastatic adenocarcinoma of the colon or rectum. Patients must have a CALGB performance score of 3 or less, a life expectancy of greater than 2 months, and adequate hematologic, renal, and liver function. Patients must not be over 75 years of age.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Spirogermanium, SPG, NSC-192965.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematological parameters, hepatic and renal function studies, blood glucose, chest x-ray, EKG.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Up to 30 eligible patients will be treated.

DOSAGE SCHEDULE:

SPG - 50 mg/sqm iv infusion over 30 minutes, q other day for 3 doses/week for 2 weeks, then twice weekly for 2 weeks, then once weekly until evidence of objective progression of disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: SPG - 100 mg vials.

DATE SUMMARIZED: 07/80

2.0065 PHASE II PILOT CHEMOTHERAPY WITH PCNU FOR ADVANCED COLON AND RECTAL ADENOCARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America

PROTOCOL NUMBER(S) EST-PC-280

OBJECTIVES:

I. Determine the response rate of measurable colonic and rectal adenocarcinoma to PCNU administered by a single-bolus iv schedule.

II. Define the qualitative and quantitative toxicity and reversibility of toxicity of PCNU administered in this fashion.

PROTOCOL ENTRY CRITERIA: Patients 16 years of age or older with measurable and histologically confirmed metastatic or recurrent adenocarcinoma of the colon and rectum; the tumor must be beyond hope of surgical eradication. Expected survival must be at least 3 months and the performance status (EST) 0, 1 or 2. Patients may have undergone major surgery, one prior chemotherapy regimen, or no treatment at all.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PCNU, NSC-95466.

STRATIFICATION BY: Participating institutions; prognostic risk: good vs. poor.

SPECIAL STUDY PARAMETERS: Measurement of indicator lesions, electrolytes, chest x-ray, liver scan, urine analysis.

END POINTS: Remission/response rate, duration of response, length of survival, quality of survival, toxicity/morbidity of treatment, objective tumor response, death.

CURRENT STATUS: 30 patients will be entered within 18 months.

DOSAGE SCHEDULE:

PCNU - 100 mg/sqm (good-risk patients), 75 mg/sqm (poor-risk patients) iv infusion over 30 minutes. Repeat q 6 weeks. Patients considered at poor risk are those with significant previous treatment with nitrosoureas, Mitomycin-C, or Dibromodulcitol or those given radiation therapy involving more than one-third of the marrow-containing skeleton. All patients receive a minimum of 2 courses; treatment is continued indefinitely unless progression or unmanageable toxicity occur.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PCNU - 50 mg vials.

DATE SUMMARIZED: 09/80

2.0066 5-FLUOROURACIL (5-FU) VS 5-FU WITH METHYL CCNU OR HYDROXYUREA FOLLOWING RESECTION OF METASTATIC COLORECTAL CARCINOMA

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PROTOCOL NUMBER(S) EST-1276

OBJECTIVES:

I. Determine the effect of chemotherapy with 5-fluorouracil alone or in combination with methyl CCNU or hydroxyurea for colorectal cancer with non-measurable, intra-abdominal metastases.

PROTOCOL ENTRY CRITERIA: Patients with 'palliative' resected primary Dukes D colorectal carcinoma with unresectable, nonmeasurable, histologically-proven, intra-abdominal metastases who have a performance status below 3 and an expected survival of at least 3 months, and who are able to begin chemotherapy from 3 to 6 weeks postsurgery (up to 60 days postsurgery if patient has undergone abdominoperineal resection. Addendum, November, 1976). Patients must not have had previous chemotherapy, second active malignancy, measurable hepatomegaly, leukopenia and thrombocytopenia, renal disease with azotemia, or significant impairment of renal function.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 2-Drug Combination Chemotherapy. 5-FU; Methyl CCNU, MeCCNU, NSC-95441.

Arm III: 2-Drug Combination Chemotherapy. 5-FU; Hydroxyurea, HU, NSC-32065.

STRATIFICATION BY: Participating institutions; location of primary: colon vs. rectum; grade of anaplasia: well-differentiated vs. moderately-differentiated vs poorly or undifferentiated; location of unresectable metastases: liver vs. other; performance status: 0 or 1 vs. 2.

SPECIAL STUDY PARAMETERS: Liver and kidney function tests, CEA, liver scan, sigmoidoscopy or colonoscopy, barium enema.

END POINTS: Time to progression, length of survival, response/remission rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

ARM I: 5-FU - 450 mg/sqm/day iv for 5 days q 5 weeks.

Arm II: 5-FU - 325 mg/sqm/day on days 1 through 5 and on days 36 through 40; MeCCNU - 150 mg/sqm po on day 1. Repeat course q 10 weeks.

Arm III: 5-FU - 600 mg/sqm iv on day 1 q week; HU - 2400 mg/sqm/day given in 4 divided doses po on day 4 q 7 days. Continue therapy until first evidence of disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg vials; MeCCNU - 10, 20, 50 and 100 mg capsules; HU - 500 mg capsules.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 02030878

2.0067 PHASE II-III CHEMOTHERAPY WITH PZD, L-PAM, MTX, ICRF-159, ACT-D, YOSHI 864, OR CCNU FOR ADVANCED LARGE BOWEL CANCER

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America

PROTOCOL NUMBER(S) EST-1277

OBJECTIVES:

I. Determine whether significant, useful activity against colonic and rectal adenocarcinoma can be demonstrated (in terms of toxicity, response rate, duration of response, duration of survival and quality of survival) as a result of treatment with the following: piperazinedione (PZD), melphalan (L-PAM), methotrexate (MTX), ICRF-159, actinomycin-D (ACT-D), Yoshi-864 or CCNU (Addendum 2, May 1979). Continuation of this master protocol can be found in EST-1277R.

PROTOCOL ENTRY CRITERIA: Patients with nonresectable confirmed metastatic or recurrent adenocarcinoma of the colon or rectum with an ECOG performance status less than 4 and an expected survival of at least 60 days. Radiotherapy for local control must be completed, chemotherapy stopped at least 28 days ago and surgery performed at least 2 weeks previously. Adequate hematological, liver and kidney functions are required.

PROTOCOL OUTLINE: Randomized study. Randomize patients with prior therapy to Arms I, IV or VI only.

Single-agent Chemotherapies.

Arm I: Piperazinedione, PZD, NSC-135758.

Arm II: Melphalan, L-PAM, NSC-8806.

Arm III: Methotrexate, MTX, NSC-740.

Arm IV: ICRF-159, NSC-129943.

Arm V: Actinomycin-D, ACT-D, NSC-3053.

Arm VI: Yoshi 864, Yoshi, NSC-102627.

Arm VII: CCNU, NSC-79037.

STRATIFICATION BY: Site of indicator lesion: liver vs. lung vs. other; ECOG performance status: 0 to 1 vs. 2 or 3; prior chemotherapy.

SPECIAL STUDY PARAMETERS: Liver function tests, skin tests, liver scan.

END POINTS: Response/remission rate, objective tumor response, duration of response, duration of survival, quality of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: PZD - 12 mg/sqm iv push every 21 days.

Arm II: L-PAM - 9.0 mg/sqm/day (maximum dose 100 mg) po for 4 days q 42 days.

Arm III: MTX - 40 mg/sqm iv on day 1, 60 mg/sqm iv on day 8 and q 7 days thereafter.

Arm IV: ICRF-159 - 1.0 mg/sqm/day for 3 days in 3 divided doses. Repeat course q 3 weeks.

Arm V: ACT-D - 2.0 mg/sqm iv push once q 28 days. Repeat course q 4 weeks.

Arm VI: Yoshi - 74 mg/sqm/day iv push for 5 days q 6 weeks.

Arm VII: CCNU - 130 mg/sqm po q 6 weeks for a minimum of 2 courses.

For all Arms, give a minimum of 6 to 8 weeks of therapy. Patients with objective progression of 3 to 4 weeks may be removed from study; keep responders and stable patients on study until disease progression. Upon failure, if patients still fulfill entry criteria, rerandomize patients to alternate Arms. Follow up all patients until death.

Dosage modifications for toxicity and patients with prior radiotherapy above 4000 rads are given.

DOSAGE FORMS: PZD - 5 mg vials; L-PAM - 2 mg tablets; MTX - 5 mg vials; ICRF-159 - 50 mg, 250 mg, and 500 mg tablets; ACT-D - 0.5 mg vials; Yoshi 864 - 100 mg vials.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 01900778

2.0068 PHASE II-III CHEMOTHERAPY WITH MEGAG OR CLZ OR AMSA OR CTX/VCR/MTX FOR COLORECTAL ADENOCARCINOMA

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PROTOCOL NUMBER(S) EST-1277R

OBJECTIVES:

I. Determine whether significant, useful activity against colorectal adenocarcinoma can be demonstrated in terms of toxicity, response rate, duration of response, duration of survival, and quality of survival as a result of treatment with methyl-GAG or chlorozotocin or m-AMSA or combination chemotherapy with cyclophosphamide/vincristine/methotrexate. Protocol EST-1277R is a continuation of the Master Protocol EST-1277.

PROTOCOL ENTRY CRITERIA: Patients with nonresectable, measurable and histologically confirmed, metastatic or recurrent adenocarcinoma of the colon and rectum. Patients must have an expected survival of at least 90 days and an ECOG performance status of 0 or 1; renal, hepatic, and hematologic functions must be adequate. Patients must have no evidence of malnutrition, severe nausea, frequent vomiting or significant infection; they must have recovered from the effects of surgery and be at least 2 weeks postoperative (3 weeks if bowel resection, anastomosis or bypass had been performed). Protocol is primarily for untreated patients, but patients may have received a single agent or a single combination of drugs prior to entry. Patients who received more than 4000 rads in prior radiotherapy are eligible but may receive a reduced initial dose. Patients must receive no chemotherapy for 4 weeks prior to entry (7 weeks if nitrosoureas, mitomycin-C or similar agents are involved).

PROTOCOL OUTLINE: Randomized study. Prior chemotherapy affects randomization: patients with prior mitomycin-C (or streptozotocin, Addendum 1, December 1979) treatment are ineligible for Arm IX; those with prior cyclophosphamide, vincristine, or methotrexate are ineligible for Arm X. Patients with no prior chemotherapy who show progression or relapse following partial or complete regression following treatment on an arm of this protocol (who still fit the criteria for inclusion) may be crossed over (re-randomized) onto a second treatment arm.

Arm VIII: Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

Arm IX: Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

Arm X: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740. Low-dose schedule or high-dose schedule. (Low-dose schedule discontinued; all patients receive high-dose schedule, Addendum 1, December 1979.)

Arm XI: Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Site of indicator lesion: hepatic vs. pulmonary vs. other; ECOG performance status: 0 vs. 1; prior chemotherapy: yes vs. no; participating institutions.

SPECIAL STUDY PARAMETERS: Measurement of indicator lesions; hematologic, hepatic, and renal function tests; chest x-ray; liver scan if indicated.

END POINTS: Response rate, duration of response, toxicity of treatment, duration of survival, quality of survival.

CURRENT STATUS: 35 patients per arm will be entered over a 4.5-year period.

DOSAGE SCHEDULE:

Arm VIII: MeGAG - 500 mg/sqm iv infusion over 45 minutes, repeated weekly with increments of 50 mg/sqm (if no toxicity is encountered) to a maximum dose of 700 mg/sqm. MeGAG may also be given by deep im injections.

Arm IX: Low-dose CLZ - 120 mg/sqm rapid iv injection on day 1, repeated q 6 weeks, or high-dose CLZ - 175 mg/sqm rapid iv injection on day 1, repeated q 6 weeks. (All Arm IX patients receive high-dose CLZ, Addendum 1, December 1979.) If at the end of 6 weeks there is not adequate hematologic or biochemical recovery, treatment is delayed.

Arm X: CTX - 300 mg/sqm iv q week; VCR - 1.4 mg/sqm (maximum dose 2.0 mg) iv q week; MTX - 25 mg/sqm iv q week.

Arm XI: AMSA - 120 mg/sqm iv infusion over 1 hour on day 1, repeated on day 29 provided recovery from myelosuppression is complete. Patients with prior Radiotherapy receive 90 mg/sqm. All patients are treated for 56 days (2 courses); patients continue on therapy until progression or unmanageable toxicity.

When possible, 6 to 8 weeks of therapy should be given. If there is progression at the end of 3-4 weeks, patients go off protocol. Patients showing a response should continue treatment until progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeGAG - 1.0 g vials; CLZ - 50 mg vials; CTX - 200 and 500 mg vials, 25 and 50 mg tablets (100 tablets/bottle); VCR - 1 and 5 mg ampules; MTX - 50 mg vials; AMSA - 75 mg ampules.

DATE SUMMARIZED: 12/80

2.0069 PHASE II COMBINATION CHEMOTHERAPY WITH 5-FU/MTX/CF/MITO FOR METASTATIC OR RECURRENT NONRESECTABLE COLORECTAL ADENOCARCINOMA

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PROTOCOL NUMBER(S) NCOG-3C91

OBJECTIVES:

I. Evaluate the objective response rate for a combination of 5-fluorouracil (5-FU), methotrexate (MTX), citrovorum factor (CF), and mitomycin-C (MITO).

II. Study the toxicity of this regimen.

III. Evaluate the duration of response to this regimen.

PROTOCOL ENTRY CRITERIA: Patients between 16 and 85 years of age with histologically confirmed, nonresectable, measurable metastatic or locally recurrent adenocarcinoma of the colon or rectum. Expected survival of at least 60 days and a performance status of 40 percent or better (Karnofsky) are required. There must be adequate renal, hepatic, and bone marrow function. Patients must have recovered from any effects of major surgery or be at least 2-3 weeks postoperative. There must be no significant detectable infection. Patients must have received no prior chemotherapy with the study drugs; short-course 5-FU (5 g/sqm or less) will be allowed. There must be no evidence of severe malnutrition, severe nausea, or frequent vomiting, and no evidence of an active second type of tumor.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; Citrovorum Factor (Leukovorin), CF, NSC-3590; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: CAT scan; bone, liver, and brain scans; chest x-ray; CEA.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 25 patients will be entered over 6 months.

DOSAGE SCHEDULE:

MTX - 60 mg/sqm po q week in 2 divided doses; CF - 80 mg/sqm/day in 4 divided doses po q week, initial dose 24 hours after MTX initial dose; 5-FU - 500 mg/sqm iv bolus q week; MITO - 10 mg/sqm iv bolus q 8 weeks only, beginning week one. Therapy will proceed for a 2-year period. Patients who show disease progression go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 25 mg tablets; CF - 5 mg tablets; 5-FU - 500 mg ampules; MITO - 5 mg vials.

DATE SUMMARIZED: 10/80

2.0070 ADJUVANT COMBINATION CHEMOTHERAPY WITH 5-FU/MECCNU/VCR OR IMMUNOTHERAPY WITH BCG FOR RESECTED COLON CARCINOMA

Fisher, B., (412-624-2671) National Surgical Adj. Breast Project, 3550 Terrace St., Room 910A, Pittsburgh, Pennsylvania, 15261, United States of America
PROTOCOL NUMBER(S) NSABP-C01

OBJECTIVES:

I. Obtain information to define subsets of colon cancer patients at high risk of recurrence.

II. Correlate pathologic and biologic parameters with disease-free interval and survival.

III. Determine the value of surgical and ancillary techniques in management of colon cancer.

IV. Compare disease-free interval and survival after curative resection vs. chemotherapy with 5-fluorouracil (5-FU)/methyl-CCNU (MeCCNU)/vincristine (VCR) vs. BCG immunotherapy.

V. Relate the total lymphocyte count to the course of the disease.

VI. Determine the feasibility of conducting a trial employing immunotherapy in a surgical adjuvant setting.

VII. Identify appropriate future protocols based on data generated in the study.

PROTOCOL ENTRY CRITERIA: Patients with potentially curable resection of colon carcinoma located above the peritoneal reflection and: (1) confined to the muscular coats of the bowel without extension into pericolic tissues or lymph nodes; (2) invading colon wall or with invasion of any depth with extension to regional lymph nodes. Patients must be 75 years of age or less, with a performance status of 0, 1, or 2 and adequate hepatic, renal and bone marrow function. Patients must not have distant metastases and have no prior history of malignancy. Patients must not have received antineoplastic agents within 6 months of entry nor prior radiotherapy to tumor area.

PROTOCOL OUTLINE: Randomized study. Enter all patients with Dukes A and D lesions to Arm I and follow up only.

Arm I: No therapy following surgery.

Arm II: 3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Methyl-CCNU, MeCCNU, NSC-95441; Vincristine, VCR, NSC-67574.

Arm III: Immunotherapy. BCG-Pasteur, BCG, NSC-B116328.

STRATIFICATION BY: Participating institutions, sex, stage of disease for Dukes B and C lesions.

SPECIAL STUDY PARAMETERS: CEA, skin tests for recall antigens, sigmoidoscopy, proctoscopy, IVP.

END POINTS: Disease-free interval, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: About 800 patients will be entered in 2 years.

DOSAGE SCHEDULE: Enter all patients within 21 and 42 days following surgery. Follow up all patients q 3 months.

Arm I: No therapy.

Arm II: VCR - 1 mg/sqm (maximum dose 2 mg) iv on days 1 and 36 prior to other agents. 5-FU - 325 mg/sqm iv on days 1 through 5 and 375 mg/sqm iv on days 36 through 40; MeCCNU - 130 mg/sqm po on day 1. Repeat course q 10 weeks for 8 courses or until progressive disease or unresolved toxicity.

Arm III: BCG - 6 x 10 to the eighth live organisms. Repeat once a week for 3 months then q other week.

Patients who fail therapy are treated at discretion of investigator.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCG - vials containing 6 x 10 to the eighth viable units; MeCCNU - 10, 50 and 100 mg capsules; VCR - 1 and 5 mg ampules; 5-FU - 500 mg ampules.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 01541278

2.0071 ADJUVANT CHEMOTHERAPY WITH 5-FU/MECCNU/VCR OR RADIOTHERAPY FOR RESECTABLE RECTAL CARCINOMA

Fisher, B., (412-624-2671) National Surgical Adj. Breast Project, 3550 Terrace St., Room 910A, Pittsburgh, Pennsylvania, 15261, United States of America

PROTOCOL NUMBER(S) NSABP-R01

OBJECTIVES:

I. Obtain information to define subsets of rectal cancer patients at high risk of recurrence.

II. Correlate pathologic and biologic parameters with disease-free interval and survival.

III. Determine the value of surgical and ancillary techniques in management of rectal cancer.

IV. Compare disease-free interval and survival after curative resection and postoperative radiotherapy or chemotherapy with 5-fluorouracil (5-FU/methyl-CCNU (MeCCNU)/vincristine (VCR).

V. Relate the total lymphocyte count to the course of the disease.

PROTOCOL ENTRY CRITERIA: Patients with potentially curative resection of rectal carcinoma located at or distal to the peritoneal reflection and: (1) confined to the muscular wall of the bowel without extension into pericolic tissues or lymph nodes; (2) invading the rectal wall with extension to pericolic tissue but without extension to lymph nodes; or (3) with invasion at any depth with extension to regional lymph nodes. Patient must be 75 years old or less with a performance status of 0, 1 or 2 and adequate renal, hepatic and bone marrow function. Patients must be free of distant metastases and have no prior history of malignancy. Patients must not have received antineoplastic agents within 6 months of entry nor prior Radiotherapy to tumor area.

PROTOCOL OUTLINE: Randomized study. Enter all patients with Dukes A or D lesions to Arm I and follow up. All other patients are randomized following Surgery.

Arm I: No therapy following surgery.

Arm II: Postsurgical Radiotherapy. Megavoltage, Co-60, 4 to 10 MeV.

Arm III: 3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Methyl CCNU, MeCCNU, NSC-95441, Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Participating institutions; stage of disease for Dukes B and C lesions, sex.

SPECIAL STUDY PARAMETERS: CEA, skin tests for recall antigens, sigmoidoscopy, proctoscopy, IVP.

END POINTS: Disease-free interval, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: About 600-800 patients will be entered in 3-5 years.

DOSAGE SCHEDULE:

Arm I: No therapy.

Arm II: Radiotherapy. Enter all patients 21 to 75 days after Surgery. Follow up all patients q 3 months - 700 to 4000 rad central midline dose, plus perineal or lateral radiation given over a period of 4 weeks.

Arm III: Enter patients 21 to 42 days after surgery. VCR - 1 mg/sqm (maximum 2 mg) iv on days 1 and 36 prior to other chemotherapeutic agents; 5-FU - 325 mg/sqm iv on days 1 through 5 and 375 mg/sqm iv on days 36 through 40; MeCCNU - 130 mg/sqm po on day 1. Repeat course q 10 weeks for 8 courses.

Patients who fail therapy are treated at the discretion of the investigator.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeCCNU - 10, 50 and 100 mg capsules; VCR - 1 and 5 mg ampules; 5-FU - 500 mg ampules.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 00511278

2.0072 RADIOTHERAPY ALONE OR WITH 5-FU/MECCNU CHEMOTHERAPY FOR RESIDUAL, NONRESECTABLE OR RECURRENT CARCINOMA OF THE RECTUM

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) RTOG-7616

OBJECTIVES:

I. Evaluate the effectiveness of the combination of standard-dose radiotherapy with added adjuvant 5-fluorouracil (5-FU), followed by maintenance chemotherapy with methyl-CCNU (MeCCNU) and 5-FU vs. high-dose radiotherapy alone by standard techniques for residual or inoperable carcinoma of the rectum and rectosigmoid or pelvic recurrence following colorectal surgery.

II. Determine the percentage and length of local control of disease, disease-free and total survival times in the various groups of patients with evaluation of mode and cause of death, interval and site of each type of failure whether local, regional and/or distant.

III. Determine the morbidity resulting from the single or combined therapies, and their effect on CEA levels, and on operability of responders.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven inoperable or residual carcinoma of the rectum or rectosigmoid or with pelvic recurrence following surgery for colorectal carcinoma without evidence of distant metastases. Patients must be ambulatory with a Karnofsky status of 60% or better and adequate blood counts. Tumor may be surgically explored or not and must be encompassed by delineated radiation fields. Patients may not have received prior 5-FU therapy of more than 10 grams.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy.

Arm II: Single-agent Chemotherapy plus Radiotherapy. 5-Fluorouracil, 5-FU, NSC-19893. Followed by Maintenance Combination Chemotherapy. 5-FU; Methyl-CCNU, MeCCNU, NSC-95441.

STRATIFICATION BY: Participating institutions, Karnofsky performance status, extent of disease, disease status (residual vs. inoperable vs. recurrent), prior 5-FU therapy.

SPECIAL STUDY PARAMETERS: Liver function tests, CEA, sigmoidoscopy, barium enema, flat state of abdomen-pelvis.

END POINTS: Response/remission, recurrence rate, objective tumor response, toxicity/morbidity of treatment, disease-free interval, survival time, CEA levels, operability of responders.

CURRENT STATUS: About 80 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 4500-5100 rads given in 5-6 weeks, plus boost fields of 7000 rads maximum given in 8 weeks. Give no further treatment until recurrence or metastases are documented.

Arm II: Radiotherapy as in Arm I, except that the maximum allowable boost field dose is 6000 rads given in 7 weeks. 5-FU - 500 mg/sqm iv for first 3 days of radiation, within 2 hours prior to radiation treatment.

Maintenance Chemotherapy: Begin 4-8 weeks after completion of Radiotherapy. 5-FU - 300 mg/sqm iv on days 1 through 5. MeCCNU - 100 mg/sqm po on day 1.

Repeat 5-FU q 5 weeks with dosages alternating between 575 and 525 mg/sqm, beginning in the second course with 575 mg/sqm. Repeat MeCCNU q 10 weeks, escalating 2nd and subsequent doses to 130 mg/sqm with MeCCNU therapy to coincide with lower alternating 5-FU dose. Continue therapy for responders without recurrence or metastases for 18 months. Follow all patients q 3 months for 5 years, then once a year until death or for 10 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00431278

2.0073 PION RADIOTHERAPY VS CONVENTIONAL RADIOTHERAPY AND SURGERY FOR NONRESECTABLE ADVANCED ADENOCARCINOMA OF THE RECTUM OR RECTOSIGMOID

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PROTOCOL NUMBER(S) RTOG-7825

OBJECTIVES:

I. Determine the effect of pion radiotherapy as compared to conventional radiotherapy upon local control of advanced adenocarcinomas of the rectum or rectosigmoid, on the incidence of complications and injury of normal tissues (bowel, bladder, skin, subcutaneous structures), on the occurrence of tumor shrinkage, sufficient to render an inoperable (or unresectable) cancer operable and potentially curable, and for re-explored cases, on the rate of regional node sterilization, and on the adjusted survival rate at 1, 2, and 3 years post radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients between the ages of 18 and 75 with biopsy proven adenocarcinoma of the rectum or rectosigmoid which is inoperable, resectable or recurrent following surgery. Patients must have a Karnofsky performance status under 60, must not have distant metastases or prior radiotherapy to the primary tumor region or prior chemotherapy within 7 days of study entry.

PROTOCOL OUTLINE: Randomized study.

Arm I: Conventional Radiotherapy plus Surgery. Cobalt-60 or other equipment of energies greater than 4 MeV. Surgery in eligible patients.

Arm II: Pion Radiotherapy plus Surgery. Surgery in eligible patients.

STRATIFICATION: Disease status: inoperable or nonresectable vs. recurrent.

SPECIAL STUDY PARAMETERS: IVP, barium enema, lymphangiogram, cystogram, liver scan, cardiopulmonary status, proctosigmoidoscopy, skin tests.

END POINTS: Response/remission rate, survival time, toxicity/morbidity of treatment, quality of life, recurrence rate, incidence of metastases.

CURRENT STATUS: 150 patients will be entered in 2 to 3 years.

DOSAGE SCHEDULE:

Arm I: 4500-5100 rad given in 5 to 6 weeks to primary tumor and adjacent tissue, including pelvic lymph node drainage area and that along the superior hemorrhoidal vessels. Evaluate patient for surgical cure and perform resection on eligible patients in 3 to 4 weeks. Enter patients ineligible for surgery to further radiotherapy of 5000-6500 rad in 6 to 7 weeks.

Arm II: Pion radiotherapy: 2000 rad minimum prior peak rad dose given in 24 days to the primary tumor and local lymphatic spread. Evaluate patient for surgery and perform resection on eligible patients in 3 to 4 weeks. Enter patients ineligible for surgery to an additional minimum of 1300 rad peak pion radiotherapy boost to the primary tumor and any known gross disease.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 11/79

2.0074 ADJUVANT CHEMOTHERAPY WITH 5-FU AND BCG IMMUNOTHERAPY FOR CURATIVELY RESECTED DUKES B2 AND C COLON CARCINOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America

PROTOCOL NUMBER(S) SEG-79GI345

OBJECTIVES:

I. Determine the overall survival, disease-free interval, recurrence (local and major) rate for carcinoma of the colon in patients with Dukes B2 and C staged tumors who underwent resection of all grossly detectable tumor with curative intent by a controlled evaluation of post-operative combined chemotherapy and immunotherapy vs. no therapy.

II. Correlate the end results for the primary objective parameters with the immunologic status (i.e. cell-mediated immunity) of the patient and determine the prognostic value of immunologic surveillance by correlating the immunologic parameters with the stage of the disease and the performance status initially and with the performance status, survival, time to recurrence, and disease-free interval during the follow-up period, and by evaluating the effect of the therapeutic modalities on those parameters.

PROTOCOL ENTRY CRITERIA: Patients with Dukes B2 or C (Stage II or III by the TNM Classification) histologically proven and curatively resected adenocarcinoma of the colon without evidence of distant metastases. Primary tumor must be located between the ileocaecal valve at its proximal margin and more than 12 cm from the anal margin. Patients must not have had prior chemotherapy or pelvic irradiation, and they must have adequate hematologic function.

PROTOCOL OUTLINE: Randomized study. Randomize patients following curative surgery and accurate staging.

Arm I: Single-agent Chemotherapy plus Immunotherapy. 5-Fluorouracil, 5-FU, NSC-19893; BCG-Tice, BCG, NSC-B116327.

Arm II: No further treatment.

STRATIFICATION BY: Type of surgery: segmental vs. subtotal vs. total colectomy vs. other surgery; sex; pathological staging: Dukes B2 vs. C1 vs C2 (C1 indicates 5 or less positive nodes, C2 indicates 6 or more positive nodes); tumor extension: confined to bowel wall and/or regional lymph nodes vs. invasive or adjacent nonlymphoid structures including pericolonic fat.

SPECIAL STUDY PARAMETERS: SMA-12, CEA, liver scan (optional), skin tests with DNCB or other recall antigens, barium enema q 12 months.

END POINTS: Disease-free interval, overall survival, recurrence rate.

CURRENT STATUS: 112 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

Enter patients within 42 days following surgery.

Arm I: 5-FU - 500 mg/sqm iv on days 1 through 5 q 28 days. Continue therapy for 72 weeks for patients remaining free of recurrences and maintaining adequate hematologic status. BCG - following skin testing with PPD, give 1 vial containing about 5 times 10 to the eighth viable units by Heaf gun divided into axilla and grain node regions on days 1, 8, 15, 22 of the first course of chemotherapy, on days 1 and 15 of course 2, on day 1 of courses 3 through 12, 15 and 18. Give first BCG course into left upper extremity, second into left lower extremity, third into right lower extremity and fourth into the right upper extremity and repeat this sequence for each succeeding course.

Arm II: No further therapy.

Follow all patients and evaluate therapy after 18 months. Then follow up responders q 3 months for 24 months and then q 6 months until death or for 6 years after the conclusion of therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; BCG - vials containing 5 times 10 to the 8th power viable units.

DATE SUMMARIZED: 07/79

2.0075 PHASE II COMBINATION CHEMOTHERAPY WITH ADR/BLEO/5-FU/MITO FOR METASTATIC EPIDERMAL CARCINOMA OF THE ANAL CANAL

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7836

OBJECTIVES:

I. Determine the antitumor effect of bleomycin (BLEO), adriamycin (ADR), mitomycin-C (MITO), and 5-fluorouracil (5-FU) as measured by response rate and survival in epidermal carcinoma of the anal canal.

II. Use the patient accrual capabilities of the Southwest Oncology Group to gather sufficient patients in this relatively uncommon tumor to arrive at a statistically valid response rate.

PROTOCOL ENTRY CRITERIA: Patients with measurable disease of histologically proven metastatic squamous cell carcinoma of the anal canal proximal to the anal verge or metastatic cloacogenic carcinoma. Patients must not have had prior chemotherapy except for initial treatment of localized disease in patients who have subsequently remained free of recurrence for 6 months or more. Serum bilirubin must not be above 5.0 mg%, and patients must have adequate renal, pulmonary and cardiac function. Poor-risk patients are those over age 65, or patients who have received more than 3000 rad to more than 25% of marrow-bearing bones within the past year.

PROTOCOL OUTLINE: Nonrandomized study.

Induction.

4-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Bleomycin, BLEO, NSC-125066; Mitomycin-C, MITO, NSC-26980; 5-Fluorouracil, 5-FU, NSC-19893.

Maintenance.

2-Drug Combination Chemotherapy. 5-FU, MITO.

STRATIFICATION BY: Disease site: transitional zone vs. anal canal elsewhere; participating institutions.

SPECIAL STUDY PARAMETERS: Pulmonary diffusion capacity, bone and liver scans, CAT or sonogram.

END POINTS: Objective tumor response, response/remission rate.

CURRENT STATUS: At least 25 patients will be entered in 16 to 20 months.

DOSAGE SCHEDULE:

Induction.

ADR - 40 mg/sqm (30 mg/sqm for poor-risk patients-PRP) iv on day 1; BLEO - 5 mg/day iv on days 1 through 5; MITO - 5 mg/sqm (4 mg/sqm for PRP) iv on day 5; 5-FU - 1,000 mg/sqm/day continuous infusion iv on days 1 through 4. Repeat course q 28 days.

Remove from study patients with increasing disease after 1 course of Chemotherapy plus 4 weeks of observation and patients with Grade 3 or 4 hematologic toxicity after one dose adjustment. Continue Induction therapy for responders or patients with stable disease until a total of 550 mg/sqm of ADR has been given, then enter patients to Maintenance. Continue therapy with BLEO until 300 mg have been given or until Induction is completed.

Maintenance.

MITO - 10 mg/sqm (7.5 mg/sqm for PRP) iv on day 1; 5-FU - 1000 mg/sqm/day continuous iv infusion on days 1 through 4, and 28 through 31. Repeat course q 56 days for 2 years past documented complete response, or until disease progression, unacceptable hematologic toxicity (see Induction), or until relapse after initial response.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MITO - 5 mg vials; 5-FU - 500 mg ampules; ADR - 10 and 50 mg ampules; BLEO - 15 mg vials.

DATE SUMMARIZED: 06/79

2.0076 PHASE II ANTI-ESTROGEN THERAPY WITH TAMOXIFEN FOR REFRACTORY LARGE BOWEL TUMORS

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7910

OBJECTIVES:

I. Investigate by response rate to tamoxifen the therapeutic significance of the laboratory observation that some colorectal tumors, in men and women, have estrogen receptor.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-confirmed measurable adenocarcinoma of the large bowel. (Biopsy for estrogen receptor status must be made before initiation of therapy. Amendment 2, April 1980) Patients must not be eligible for higher priority protocols; they may have received prior radiotherapy (and prior chemotherapy, Amendment 2, April 1980). Patients must have a performance status of 0, 1, or 2, an estimated life expectancy of at least 30 days, a granulocyte count of at least 2000, and less than 25% liver replacement by tumor.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Anti-estrogen Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Performance status: 0 or 1 vs. 2; participating institutions.

SPECIAL STUDY PARAMETERS: Estrogen receptors, CEA, x-rays of involved or painful areas, liver scan if indicated.

END POINTS: Response/remission rate, objective tumor response.

CURRENT STATUS: Estimated accrual of 2-3 patients/month for 2 years; protocol requires at least 25 response-evaluable ER+ (and 25 ER-) patients.

DOSAGE SCHEDULE:

TMX - 80 mg/sqm/day po in 2 divided doses for 7 days, then 20 mg/sqm/day as long as there is tumor regression or acceptable stability.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: TMX - 5 and 10 mg tablets.

DATE SUMMARIZED: 08/79

2.0077 CONTROL ARM OF A COMPARISON OF VARIOUS PHASE II AGENTS VS 5-FU FOR DISSEMINATED OR RECURRENT COLORECTAL CARCINOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7940

OBJECTIVES:

I. Provide control data for the comparison of various Phase II agents with standard 5-fluorouracil chemotherapy in patients with disseminated or recurrent adenocarcinoma of the colon and rectum. (See also SWOG-7940/41 and SWOG-7940/43).

II. Determine the effect of a previously administered Phase II drug on the response rate seen with 5-fluorouracil among patients who fail or relapse on the Phase II agents and are crossed to standard chemotherapy.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with biopsy-proven adenocarcinoma of the colon or rectum who have clinically measurable disease. Patients must have a life expectancy of at least 10 weeks and a performance status of not worse than 2 by SWOG criteria. Marrow function must be adequate. At least 3 weeks must have elapsed since prior surgery.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Sex, prognostic risk (good vs. poor), performance status (0-1 vs. 2), participating institutions.

SPECIAL STUDY PARAMETERS: Performance status, hemogram, kidney and liver function tests, CEA, x-rays and scans as appropriate for tumor assessment.

END POINTS: Response/remission rate, duration of response, objective tumor response.

CURRENT STATUS: 30-40 patients will be entered in about 4 months.

DOSAGE SCHEDULE:

5-FU - 550 mg/sqm (400 mg/sqm in poor-risk patients) iv bolus on days 1 through 5. Repeat course in 4 weeks. If no myelosuppression at 4 weeks, increase dose for good-risk patients to 600 mg/sqm.

Continue responders until progression, unsatisfactory stable disease, or unacceptable toxicities. Cross to a Phase II agent those who fail and those who relapse after response.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules.

DATE SUMMARIZED: 08/80

2.0078 PHASE II EVALUATION OF METHYL-GAG AS FIRST LINE CHEMOTHERAPY IN PATIENTS WITH RECURRENT OR DISSEMINATED COLORECTAL CARCINOMA

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PROTOCOL NUMBER(S) SWOG-7940/41

OBJECTIVES:

I. Determine the efficacy of methyl-GAG (MeGAG) in the treatment of previously untreated patients with recurrent or disseminated colorectal carcinoma.

II. Compare the survival of these patients with that of those treated with 5-fluorouracil as first therapy (SWOG-7940).

III. Determine the effect of previously administered methyl-GAG on the response rate seen with 5-fluorouracil after crossing failures on methyl-GAG to 5-fluorouracil (SWOG-7940).

PROTOCOL ENTRY CRITERIA: Previously untreated patients with biopsy-proven recurrent or disseminated adenocarcinoma of the colon or rectum whose disease is clinically measurable. Patients must have a life expectancy of at least 10 weeks and a performance status of not worse than 2 by SWOG criteria. Marrow reserves must be adequate, and at least 3 weeks must have elapsed since prior surgery.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

STRATIFICATION BY: Sex, performance status (0-1 vs. 2), prognostic risk (good vs. poor), participating institutions.

SPECIAL STUDY PARAMETERS: Performance status, tumor measurement, hemogram, renal and hepatic function tests, chest x-ray, other x-rays and scans indicated clinically.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 30-40 patients will be entered in approximately 4 months.

DOSAGE SCHEDULE:

MeGAG - 600 mg/sqm by iv infusion over 30 minutes. Repeat weekly. In the absence of gastrointestinal and hematologic toxicity, increase dose by 100 mg/sqm. Continue until progression, unsatisfactory stable disease, or unacceptable toxicity. Cross failures to standard 5-fluorouracil treatment (SWOG-7940).

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeGAG - 1 g vials.

DATE SUMMARIZED: 08/80

2.0079 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE FOR PREVIOUSLY UNTREATED RECURRENT OR METASTATIC CARCINOMA OF THE COLON OR RECTUM

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PROTOCOL NUMBER(S) SWOG-7940/43

OBJECTIVES:

I. Determine the efficacy of treatment with gallium nitrate in previously untreated patients with colorectal carcinoma.

II. Compare the survival of these patients receiving gallium nitrate as a first therapy to that of patients receiving 5-fluorouracil as a first therapy (SWOG-7940).

III. Determine the effect of prior treatment with gallium nitrate on the response rate to 5-fluorouracil among patients who fail on gallium nitrate and are crossed to 5-fluorouracil (SWOG-7940).

PROTOCOL ENTRY CRITERIA: Previously untreated patients with biopsy-proven adenocarcinoma of the colon or rectum who have clinically measurable recurrent or disseminated disease. Patients must have a life expectancy of at least 10 weeks and a performance status (SWOG) of at worst Grade 2. Marrow function must be adequate. A period of at least 3 weeks should intervene between prior surgery and initiation of chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Gallium nitrate, GAN, NSC-15200.

STRATIFICATION BY: Participating institutions, prognostic risk (good vs. poor), performance status (0-1 vs. 2), sex.

SPECIAL STUDY PARAMETERS: Performance status, hemogram, liver and kidney function tests, CEA, appropriate x-rays and scans to follow lesions.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment, audiogram.

CURRENT STATUS: Forty patients will be entered.

DOSAGE SCHEDULE:

GAN - 700 mg/sqm by 30-minute iv infusion. Repeat q 2 weeks. Prehydrate with 2 liters in excess of normal intake during 24 hours prior to drug administration. Continue until tumor progression, unsatisfactory stable disease, or unacceptable toxicity. Cross failures to 5-fluorouracil (SWOG-7940).

Dosage modifications for toxicity are given.

DOSAGE FORMS: GAN - 100 mg ampules.

DATE SUMMARIZED: 08/80

2.0080 PHASE II EVALUATION OF DIHYDROXYANTHRACENEDIONE IN PATIENTS WITH COLORECTAL CARCINOMA

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United States of America
PROTOCOL NUMBER(S) SWOG-7944

OBJECTIVES:

I. Determine the response rate and duration of response of patients with colorectal cancer treated with dihydroxyanthracenedione as a single dose q 3 weeks.

II. Evaluate the qualitative and quantitative toxicities associated with this treatment.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven colorectal carcinoma who have clinically measurable, recurrent or disseminated disease and who have not received prior chemotherapy. Life expectancy must be at least 10 weeks, the performance status no worse than Grade 2 by SWOG criteria, and the bone marrow function adequate. At least 3 weeks must have intervened between surgery and the beginning of chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Sex, performance status (0-1 vs. 2), prognostic risk (good vs. poor), participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, blood glucose, chest x-ray, EKG, appropriate scans and/or x-rays.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: About 50 patients will be entered on this treatment arm.

DOSAGE SCHEDULE:

DHAD - 12 mg/sqm iv over 30 minutes repeated at 21-day intervals. If WBC nadir is at least 4000 and platelet nadir at least 100, 000, escalate dosage by 10 percent. An adequate trial will consist of 2 courses. Failures will be crossed over to standard 5-Fluorouracil therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

2.0081 ADJUVANT PHASE II-PILOT CHEMOTHERAPY WITH MITO/5-FU PLUS RADIOTHERAPY FOR HIGH-RISK PATIENTS WITH RESECTED COLON CARCINOMA

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PROTOCOL NUMBER(S) SWOG-8066

OBJECTIVES:

I. Determine the toxicities of combined intra-arterial chemotherapy with mitomycin-c (MITO) and 5-fluorouracil (5-FU) plus hepatic radiotherapy after total clinical resection of cancer of the colon in patients who have a high risk of recurrence (Dukes C), for potential use in an adjuvant Group-wide protocol.

PROTOCOL ENTRY CRITERIA: Patients with completely resected adenocarcinoma of the colon, with involvement of adjacent regional lymph nodes (patients with carcinoma of the rectum are ineligible). Patients must not have received prior chemotherapy or radiotherapy. Prior surgical decompression is acceptable but only one attempt at resection of all gross tumor is permitted. Patients must have normal hepatic and renal function.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy plus Radiotherapy. Mitomycin-C, MITO, NSC-26980; 5-Fluorouracil, 5-FU, NSC-19893; plus megavoltage irradiation, Cobalt-60 gamma rays or x-ray beams with peak energy 2 MeV or greater.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: CEA, chest x-ray, barium enema, liver scan.

END POINTS: Recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 20 patients will be entered.

DOSAGE SCHEDULE:

MITO - 3 mg/sqm by slow intra-arterial push (via catheter placed in the hepatic artery percutaneously) on days 1, 4, 35 and 38; 5-FU - 1000 mg/sqm by continuous 96-hour intra-arterial infusion on days 1 through 4 and 35 through 38. Megavoltage irradiation beginning on day 8, 1950 rads in 13 fractions at the rate of 150 rads/day for 5 days/week for 2.5 weeks, delivered to the entire liver.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; MITO - 5 mg vials.

DATE SUMMARIZED: 10/80

2.0082 PHASE II EVALUATION OF INTRAVENOUS 6-TG IN PATIENTS WITH METASTATIC COLORECTAL ADENOCARCINOMA

Konits, P. H., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7919

OBJECTIVES:

I. Evaluate the therapeutic potential of iv 6-thioguanine in patients with metastatic colorectal cancer.

PROTOCOL ENTRY CRITERIA: Patients with easily measurable metastatic lesions from colorectal cancer who have an expected survival of at least 2 months. Patients must have completed prior chemotherapy or radiotherapy at least 4 to 6 weeks prior to entry, should be ambulatory, and should be under the age of 75.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. 6-Thioguanine, 6-TG, NSC-752.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-6, SMA-12, CEA, chest x-ray with tomography when indicated, metastatic bone survey if prior scan suggested metastasis, UGI and IVP as indicated, liver/spleen scan, brain CAT scan if metastasis is suspected, EKG.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: About 20 patients will be required to complete an initial evaluation.

DOSAGE SCHEDULE:

6-TG - 700 mg/sqm by rapid iv bolus injection. Repeat q 3 weeks for a minimum of 2 courses and continue until disease progresses. Escalate dosage by 100 mg/sqm in the absence of side effects.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

2.0083 ADJUVANT RADIOTHERAPY PLUS CHEMOTHERAPY WITH 5-FU FOR CURATIVELY RESECTED ADENOCARCINOMA OF THE COLON

Moertel, C., (507-282-2511 Ext. 3261) Gastrointestinal Tumor Study Group, 850 Sligo Ave., Suite 601, Silver Spring, Maryland, 20910, United States of America
PROTOCOL NUMBER(S) GTSG-6179; BCRP-7917

OBJECTIVES:

I. Determine whether adjuvant hepatic irradiation plus chemotherapy with 5-fluorouracil (5-FU) improves either survival or time to recurrence after potentially curative surgery of colon cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed adenocarcinoma of the colon with distal margin of tumor at least 12 cm proximal to the anal verge who have had all detectable tumor surgically excised en bloc. Patients must be ambulatory, have adequate hematologic function and maintain adequate oral nutrition, and have no wound-healing complications by 7 weeks after surgery. Patients must not have distant metastases, nor microscopic tumor involvement at margin of resection. Patients must have no acute or chronic liver disease, infection, prior chemotherapy with 5-FU or radiotherapy to thorax or abdomen, or evidence of acute or chronic renal disease or nonfunctioning left kidney.

PROTOCOL OUTLINE: Randomized study.

Arm I: Control Group. No adjuvant therapy.

Arm II: Single-agent Chemotherapy plus Radiotherapy. 5-Fluorouracil, 5-FU, NSC-19893; plus supervoltage irradiation to entire liver.

STRATIFICATION: Participating institutions; anatomic location: ascending vs. transverse vs. descending and sigmoid to peritoneal reflection; Stage: Dukes B-2 vs. C-1 serosal vs. C-1 non-serosal involvement vs. C-2; time of therapy: 2 to 4 weeks vs. 4 to 7 weeks post-operative.

SPECIAL STUDY PARAMETERS: Hematologic, liver, and kidney functions; carcinoembryonic antigen; liver scan; proctoscopy; barium enema or fiberoptic total colonoscopy.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 360 patients will be entered in 2 to 4 years.

DOSAGE SCHEDULE:

Arm I: No further treatment.

Arm II: Begin therapy within 2 to 7 weeks (preferably before 4 weeks) of surgery. 5-FU - 500 mg/sqm (revised to 350 mg/sqm, Addendum 2, May 1980) iv bolus on days 1 through 3 of Radiotherapy, then 2 weeks after completion of Radiotherapy if WBC is over 4000 - 500 mg/sqm iv push for 5 days q 4 weeks for 2 courses. Delay 5-FU for up to 2 weeks if WBC is under 4000. If WBC is over 3000 but still under 4000 by 7 weeks after previous course, reduce 5-FU to 400 mg/sqm. Hepatic irradiation: 2100 rad given 5 days/week in 150-rad fractions to the whole liver.

Follow up patients q 3 months for the first year, q 6 months for the second year, and q year thereafter for a total of 5 years. (Modified to q 6 months for years 2 through 5 by Addendum 3, July 1980.)

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/80

2.0084 PHASE II COMBINATION CHEMOTHERAPY WITH MOF-STREP (MECCNU/VCR/5-FU/SZC) FOR ADVANCED COLORECTAL CARCINOMA

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PROTOCOL NUMBER(S) GTSG-6380

OBJECTIVES:

I. Obtain confirmation of the encouraging results of MOF-Strep: methyl-CCNU (MeCCNU), vincristine (VCR), 5-fluorouracil (5-FU) and streptozotocin (SZC) in treatment of advanced colorectal carcinoma.

II. Apply the results of this study to a rational design for future adjuvant chemotherapy trials in colorectal cancer.

PROTOCOL ENTRY CRITERIA: Patients with measurable, metastatic or recurrent, histologically confirmed adenocarcinoma of the colon and rectum. The tumor must be beyond hope of surgical eradication. The expected survival must be at least 60 days, and the performance status (ECOG) 3 or better (bedridden Class 4 patients not eligible). There must have been no prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. MOF-STREP: Methyl-CCNU, MeCCNU, NSC-95441; Vincristine, VCR, NSC-67574; 5-Fluorouracil, 5-FU, NSC-19893; Streptozotocin, SZC, NSC-85998.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum creatinine, creatinine clearance, liver scan, chest x-ray, CEA.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 40 patients will be entered.

DOSAGE SCHEDULE:

MeCCNU - 30 mg/sqm po on days 1 through 5 q 10 weeks; VCR - 1 mg total iv on day 1 q 5 weeks; 5-FU - 300 mg/sqm iv on days 1 through 5 q 5 weeks; SZC - 500 mg/sqm iv over 20 minutes (50cc D5/W) q week. Repeat course every 10 weeks until progression, at which time patients are taken off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

2.0085 PHASE II-III CHEMOTHERAPY WITH FTORAFUR VS 5-FU/MECCNU/TZT VS 5-FU/MECCNU/ICRF-159 VS 5-FU/MECCNU/VCR FOR ADVANCED COLORECTAL CANCER

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PROTOCOL NUMBER(S) MAYO-764802

OBJECTIVES:

I. Compare chemotherapy with ftorafur vs. 5-fluorouracil (5-FU)/methyl CCNU (MeCCNU) combined with either triazinate (Baker's Antifol, TZT) or ICRF-159 (ICRF) or vincristine (VCR) for advanced cancer of the large bowel.

PROTOCOL ENTRY CRITERIA: Patients with measurable lesions of primary or metastatic cancer of the large bowel not amenable to conventional therapy. Patients must be ambulatory, must have adequate hematological and renal function, maintain a reasonable state of nutrition and must have a life expectancy of more than 6 weeks. Prior radiotherapy must have been limited to no more than 2500 rads to the entire pelvis and lumbosacral spine and all prior therapy must have been concluded 1 month before study entry.

PROTOCOL OUTLINE: Randomized study.

Enter all patients with prior nitrosourea therapy to Arm I. Exclude all patients with serum creatinine levels higher than 1.5 or with elevated direct reacting serum bilirubin from Arm II.

Arm I: Single-agent Chemotherapy. Ftorafur, NSC-148958.

Arm II: 3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Methyl CCNU, MeCCNU, NSC-95441; Triazinate, Baker's antifol, TZT, NSC-139105.

Arm III: 3-Drug Combination Chemotherapy. 5-FU, MeCCNU plus ICRF-159, NSC-129943.

Arm IV: 3-Drug Combination Chemotherapy. 5-FU, MeCCNU plus Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Participating institutions; ECOG performance status: 0 or 1 vs. 2 or 3; site of indicator lesion: pulmonary vs. hepatic vs. other; prior chemotherapy: any vs. none.

SPECIAL STUDY PARAMETERS: Serum CEA, circulating T and B cells, lymphocyte blastogenesis, immunoglobulins.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, duration of response, time to progression, complete/partial response rate.

CURRENT STATUS: 265 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Ftorafur - 2.5 mg/sqm/day iv on days 1 through 5 q 5 weeks. Monitor wbc and platelets on day 5, then wbc twice a week, platelets once a week.

Arm II: 5-FU - 300 mg/sqm/day iv on days 1 through 5 q 5 weeks; MeCCNU - 150 mg/sqm po on day 1 q 10 weeks; TZT - 150 mg/sqm iv on days 1, 2 and 3 and 36, 37 and 38. Monitor wbc and platelets on days 3 and 5, then wbc twice a week and platelets once a week for 10 weeks, then both once a week. Repeat course q 10 weeks.

Arm III: 5-FU - 325 mg/sqm/day iv on days 1 through 5 q 5 weeks; MeCCNU - 110 mg/sqm po on day 1 q 10 weeks; ICRF-159 - 500 mg/sqm po in 3 divided doses on days 2, 3 and 4 and 36, 37 and 38. Monitor wbc and platelets as in Arm II. Repeat course q 10 weeks.

Arm IV: 5-FU - 350 mg/sqm/day iv on days 1 through 5, 400 mg/sqm/day iv on days 36 through 40; MeCCNU - 175 mg/sqm po on day 1; VCR - 1 mg/sqm iv on days 1 and 36. Repeat course q 10 weeks. Monitor wbc and platelets on day 5 and thereafter as in Arm II.

Evaluate all patients q 5 weeks and remove patients with disease progression from study. Follow up for survival. Repeat course for patients with responding or stable measurable disease until evident disease progression. Adjust dosages to produce definite but tolerable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Ftorafur - 40 mg ampules; 5-FU, VCR - not given; MeCCNU - 10, 20, 50 and 100 mg capsules; TZT - 100 and 250 mg vials; ICRF-159 - 50, 250 and 500 mg tablets.

DATE SUMMARIZED: 02/77

PATIENT ACCRUAL: 01550279

2.0086 VITAMIN C VS PLACEBO IN PATIENTS WITH ADVANCED COLORECTAL CANCER WHO HAVE HAD NO PRIOR IMMUNOSUPPRESSIVE THERAPY

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PROTOCOL NUMBER(S) MAYO-790602

OBJECTIVES:

I. Compare the efficacy of Vitamin C with that of placebo in terms of time to progression, survival, toxicity, and symptomatic status in a double-blind study with patients having advanced cancer of the colon and rectum.

PROTOCOL ENTRY CRITERIA: Patients with advanced tissue-proven malignancies of the colon and rectum. Patients may not be eligible for chemotherapy, radiotherapy, or palliative surgery. Patients must have a performance status of 0-1 and must not have been previously treated with high-dose Vitamin C.

PROTOCOL OUTLINE: Double blind, randomized study.

Arm I: Single-agent Chemotherapy. Ascorbic Acid, VIT-C, NSC-33832.

Arm II: No treatment. Placebo is given.

STRATIFICATION BY: Time of diagnosis of unresectable malignant disease to time of study entry (less than 3 weeks, 3-8 weeks, more than 8 weeks), site of metastases (pulmonary vs. liver vs. other), measurable disease vs. nonmeasurable disease.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Time to disease progression, survival, toxicity, symptomatic status.

CURRENT STATUS: Patient accrual will be about 40 per year for 3 years.

DOSAGE SCHEDULE:

Arm I: VIT-C - 10 g/day in 4 divided doses, po. Continue until progression.

Arm II: Placebo - same number of capsules and schedule as in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: VIT-C - 500 mg capsules.

DATE SUMMARIZED: 07/80

2.0087 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED LARGE BOWEL ADENOCARCINOMA

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Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-794602

OBJECTIVES:

I. Determine the therapeutic activity of PALA in patients with advanced colorectal cancer.

PROTOCOL ENTRY CRITERIA: Patients with measurable disease of histologically proven residual, recurrent or metastatic colorectal adenocarcinoma beyond hope of cure by surgery or other potentially effective therapy. Patients must have an ECOG performance status better than 4, creatinine below 1.5, and adequate nutrition. They must not have had major surgery or chemotherapy within 4 weeks (8 weeks for nitrosoureas) nor radiotherapy to more than 15% of the bone marrow in the preceding 30 days or to more than 30% of bone marrow at any time (not over 2500 rad in 13 fractions).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Liver and CAT scans.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

PALA - 1250 mg/sqm iv infusion on days 1 through 5 q 4 weeks until disease progression.

DOSAGE FORMS: PALA - 100 mg vials.

DATE SUMMARIZED: 06/79

2.0088 PHASE II CHEMOTHERAPY WITH L-ALANOSINE FOR ADVANCED LARGE BOWEL ADENOCARCINOMA

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Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-804601

OBJECTIVES:

I. Determine therapeutic activity of L-alanosine in patients with advanced colorectal adenocarcinoma.

PROTOCOL ENTRY CRITERIA: Patients with nonresectable histologically proven colorectal adenocarcinoma (residual, recurrent or metastatic disease) for which no more potentially effective therapy is known. Disease must be measurable. Patients must have a ECOG performance status under 4 and adequate hematologic function. Patients must have no uncontrolled infectious process, severe malnutrition, nausea or frequent vomiting. Patients must not have surgery or chemotherapy within the 4 weeks prior to entry (8 weeks for nitrosoureas). Patients must not receive radiotherapy to more than 15 percent of the bone marrow within the 30 days preceding entry or to more than 30 percent at any time preceding entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. L-Alanosine, NSC-153353.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic, renal and hepatic function tests; chest x-ray.

END POINTS: Response/remission rate, objective tumor response, duration of response, survival.

CURRENT STATUS: 15 patients with prior chemotherapy and 15 patients without prior chemotherapy will be entered.

DOSAGE SCHEDULE:

L-Alanosine - 160 mg/sqm iv over 10 minutes on days 1 through 5 q 4 weeks. Patients who show progression go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-Alanosine - 10 mg vials.

DATE SUMMARIZED: 10/80

2.0089 PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE FOR METASTATIC COLORECTAL ADENOCARCINOMA

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Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-804602

OBJECTIVES:

I. Determine the therapeutic activity of aziridinylbenzoquinone in patients with advanced colorectal cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven colorectal adenocarcinoma, with a measurable area of known malignant disease. Patients must not be candidates for surgical cure or other potentially more effective therapy. Patients must have an ECOG performance status better than 4 and adequate hematologic, renal, and hepatic function. Patients must have no serious uncontrolled infectious process, malnutrition, nausea, or frequent vomiting. Patients must not undergo surgery (resection or bypass) within 4 weeks prior to entry. No chemotherapy is allowed within the 4 weeks prior to entry; patients must not have received radiotherapy to 15 percent of the bone marrow within 30 days of entry or radiotherapy to more than 40 percent of the bone marrow at any time.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Aziridinylbenzoquinone, AZQ, NSC-182986.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; tumor measurement; chest x-ray.

END POINTS: Response/remission rate, objective tumor response, duration of response, interval to progression, survival.

CURRENT STATUS: Initially, 15 patients with prior chemotherapy will be entered. Following this, 15 patients without prior chemotherapy will be entered.

DOSAGE SCHEDULE:

AZQ - 22.5 mg/sqm iv over 5-15 minutes on day 1 q 4 weeks for patients with prior chemotherapy or radiotherapy, patients over 70 years of age, and patients with a performance status of 3. Patients with no prior chemotherapy or radiotherapy, patients under 70 years of age, and patients with performance status of 0, 1, or 2 receive AZQ - 27.5 mg/sqm iv over 5-15 minutes on the same schedule. The retreatment interval may be prolonged up to 6 weeks on the basis of hematologic or clinical parameters. Patients are treated until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZQ - 10 mg vials.

DATE SUMMARIZED: 11/80

2.0090 HEPATIC AND PELVIC ARTERIAL INFUSION WITH MITO/FUDR PLUS RADIOTHERAPY AND BCG IMMUNOTHERAPY FOR DUKES C AND D1 COLON CANCER

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PROTOCOL NUMBER(S) MDAR-310; MDA-DT-7864

OBJECTIVES:

I. Determine the efficacy of hepatic arterial infusion of mitomycin-C (MITO) and floxuridine (FUDR) followed by BCG for preventing recurrence in Dukes C and Dukes D1 colon cancer in NED patients with nonrectal primary lesions.

II. Determine the feasibility and efficacy of adding radiotherapy and pelvic infusion of MITO and FUDR to Dukes C and Dl colon cancer patients whose primary lesions are in the rectosigmoid colon.

III. Determine the quantitative and qualitative toxicity of the combination of MITO and FUDR administered in this fashion.

IV. Determine whether this combination will prolong disease-free interval and survival of Dukes C and D1 colon cancer patients.

PROTOCOL ENTRY CRITERIA: Patients with Dukes C colorectal carcinoma with more than 1 involved lymph node or with Dukes D1, if the tumor extension beyond the lymph nodes and bowel wall was adjacent to the primary and has been completely resected. Removal of primary must have taken place within 6 to 8 weeks of study entry, and all patients must be NED.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with Dukes C disease to Regimen A if primary is rectosigmoid, other patients to Regimen B. Enter patients with Dukes D disease to Regimen C if primary is rectosigmoid, all others to Regimen D.

Regimen A: 2-Drug Combination Chemotherapy plus Radiotherapy plus Immunotherapy. Mitomycin-C, MITO, NSC-26980; plus Floxuridine, FUDR, NSC-27640, given via hepatic arterial infusion (HAI) and pelvic arterial infusion (PAI); plus BCG-Pasteur, BCG, NSC-B116328; plus pelvic irradiation.

Regimen B: 2-Drug Combination Chemotherapy plus Immunotherapy. MITO; FUDR via HAI; plus BCG.

Regimen C: 2-Drug Combination Chemotherapy plus Radiotherapy plus Immunotherapy. MITO; FUDR given via HAI and PAI; plus pelvic irradiation; plus BCG.

Regimen D: 2-Drug Combination Chemotherapy plus Immunotherapy. MITO; FUDR given via HAI; plus BCG.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Disease-free interval, appearance of metastases, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: About 50 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: MITO - 15 mg/sqm via hepatic arterial infusion on day 1 after the placement of hepatic arterial catheter; FUDR - 100 mg/sqm HAI on days 1 through 5. Begin Radiotherapy upon recovery from Chemotherapy; 5100 rads in 6 weeks for patients who have had an anterior resection, 4500 rads to the pelvis with a boost of 100 rads to the peritoneum for patients who have had an abdominal-perineal resection. On the completion of Radiotherapy, give one course of MITO; FUDR via HAI followed by one course of MITO; FUDR via pelvic arterial infusion; then begin BCG - 6 x 10 to the 8th organism by scarification once a week for 1 month, thereafter q 2 weeks for a total of 2 years of therapy.

Regimen B: MITO; FUDR (dosage as in Regimen A) via HAI. Give 4 courses (retreatment interval is not given). BCG - as in Regimen A.

Regimen C: MITO; FUDR (dosage as in Regimen A) via HAI; followed by Radiotherapy - 5000 rads to the pelvis; then give 2 courses of MITO; FUDR via HAI plus one course via PAI; plus BCG as in Regimen A.

Regimen D: MITO; FUDR (dosage as in Regimen A) via HAI for 5 courses (retreatment interval not given); plus BCG as in Regimen A.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/79

2.0091 CHEMOTHERAPY WITH ORAL FTORAFUR VS INTRAVENOUS 5-FLUOROURACIL FOR ADVANCED COLON AND RECTAL CARCINOMA

Bodey, G. P., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-332; MDA-DT-7920

OBJECTIVES:

I. Compare effects of single-agent chemotherapy with oral Ftorafur (FT) vs. intravenous 5-Fluorouracil (5-Fu) in approximately equitoxic doses for progressing carcinoma of the colon and rectum.

II. Determine efficacy of oral FT in patients failing to respond to intravenous 5-FU.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, progressing carcinoma of the colon or rectum who have adequate major organ function and nutrition. Patients must not have prior treatment with protocol drugs and must have recovered from toxicities of other therapy. Women of child-bearing potential must agree to an accepted method of avoiding pregnancy during participation in this study.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Ftorafur, FT, NSC-148958.

Arm II: Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: Approximately 40 patients will be entered.

DOSAGE SCHEDULE:

Arm I: FT - 1.0 gm/sqm/day (1.25-3.00 gm/sqm/day per Revision, June 1979) po in 2 divided doses on days 1 through 21.

Arm II: 5-FU - 500 mg/sqm/day iv on days 1 through 4, then 250 mg/sqm iv on days 6, 8, 10 and 12. (5-FU - 12 mg/kg/day iv for 5 days. Revision, June 1979.) Cross over to Arm I patients who show no response after 3 courses for a minimum of 2 courses on alternate therapy. Repeat courses q 4 weeks if there is no residual toxicity from preceding course.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 04/80

2.0092 PHASE II CHEMOTHERAPY WITH PALA FOR METASTATIC COLORECTAL CARCINOMA

Valdivieso, M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-350; MDA-DT-7942

OBJECTIVES:

I. Determine the efficacy of PALA, administered either by single dose or a 5-day intravenous schedule to patients with metastatic colorectal cancer.

II. Determine the qualitative and quantitative toxicity of PALA administered in this fashion.

III. Determine duration of response and duration of survival of patients receiving this therapy.

IV. Correlate clinical responses with changes in plasma levels of carcinoembryonic antigen.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with measurable disease of histologically proven metastatic colorectal adenocarcinoma not previously treated by chemotherapy. Patients must have a life expectancy of at least 12 weeks, adequate bone marrow, liver and renal function. They must have concluded all prior therapy 4 weeks before study entry and must have recovered from any toxic effects.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients to either Regimen A or Regimen B. Patients living in Houston and vicinity are preferentially entered to Regimen B.

Regimen A: Single-agent Chemotherapy. PALA, NSC-224131. Single dose schedule.

Regimen B: Single-agent Chemotherapy. PALA. Multiple dose schedule.

STRATIFICATION: Not given.

SPECIAL STUDY PARAMETERS: CEA.

END POINTS: Response/remission rate, response duration, toxicity/morbidity of treatment, survival time, objective tumor response.

CURRENT STATUS: A minimum of 30 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: PALA - 6 g/sqm iv on day 1 q 2 weeks.

Regimen B: PALA - 1 g/sqm/day iv on days 1 through 5 q 2 weeks.

Give a minimum of 4 courses on each regimen. Remove from study patients with increasing disease after 3 courses of therapy and patients with unacceptable toxicity or unsatisfactory status quo.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

2.0093 PHASE II CHEMOTHERAPY WITH PCNU FOR METASTATIC COLORECTAL ADENOCARCINOMA IN ADULTS

Bedikian, A. Y., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77025, United States of America

PROTOCOL NUMBER(S) MDAR-373; MDA-DT-7993

OBJECTIVES:

I. Determine the efficacy of PCNU administered by single dose schedule to patients with metastatic colorectal cancer.

II. Determine the qualitative and quantitative toxicity of PCNU administered in this fashion.

III. Determine duration of response and survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: All patients with histologic proof of metastatic colorectal adenocarcinoma who are not eligible for other protocol treatments of higher priority and who have had no prior treatment with nitrosoureas. Patients must have a life expectancy of at least 12 weeks, have measurable lesions, be at least 15 years old, and have adequate bone marrow, liver and renal function. They must have been off all previous therapy for the 4 preceding weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PCNU, NSC-95466.

STRATIFICATION BY: Prognostic risk.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response.

CURRENT STATUS: A minimum of 30 evaluable patients will be entered, continuation of study dependent upon efficacy of the therapy during initial phases.

DOSAGE SCHEDULE:

PCNU - 100 mg/sqm (75 mg/sqm in patients with inadequate bone marrow reserve, prior treatment with mitomycin-C, or radiotherapy to chest, spine, and pelvis) iv on day 1; 41 days of rest, then course repeated. Dosage increased or decreased as determined by granulocyte and platelet count. Total period of therapy - 1 year after achieving complete remission or 2 years maximum.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

2.0094 PHASE II CHEMOTHERAPY WITH AZQ FOR METASTATIC COLORECTAL CANCER

Bedikian, A., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-393; MDA-DT-8023

OBJECTIVES:

I. Determine the efficacy of AZQ administered on a 5-day dose schedule in patients with metastatic colorectal cancer.

II. Determine the qualitative and quantitative toxicity of AZQ administered in this fashion.

III. Determine duration of response and survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic colorectal adenocarcinoma with measurable lesions who are not eligible for higher priority protocol treatments. Patients must be at least 15 years of age; they must have a life expectancy of at least 12 weeks, and have adequate bone marrow reserve, liver function, and renal function. Patients must have received no therapy for 4 weeks prior to entry and must have recovered from the toxic effects of any previous therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. AZQ, NSC-182986.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic function tests.

END POINTS: Response/remission rate, duration of response, survival rate, length of survival, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 30 patients will be entered.

DOSAGE SCHEDULE:

AZQ - 8 mg/sqm (in good-risk patients with adequate bone marrow reserve and no prior mitomycin-C or nitrosourea therapy) iv daily for 5 days q 4 weeks, with increments of 2 mg/sqm based on granulocyte and platelet counts. Poor-risk patients (inadequate bone marrow reserve and prior chemotherapy with mitomycin-C or nitrosoureas or radiotherapy to chest, spine, and pelvis) receive an initial dose of 6 mg/sqm. All patients receive 2 courses; therapy will be continued for 2 years or for 1 year after achieving CR, whichever is shorter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/80

2.0095 IV CHEMOTHERAPY WITH DAVA/5-FU/MITO-C VS HAI CHEMOTHERAPY WITH DAVA/FUDR/MITO-C FOR COLORECTAL CARCINOMA WITH LIVER METASTASES

Patt, Y. Z., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-412; MDA-DT-8029

OBJECTIVES:

I. Determine whether repeated hepatic arterial infusion (HAI) of vindesine, mitomycin-C, and floxuridine can increase response rate, response duration, and survival of patients with colorectal carcinoma metastatic to the liver.

II. Determine the response rate, response duration, and survival of patients with colorectal carcinoma metastatic to the liver treated by hepatic arterial occlusion and systemic intravenous administration of vindesine, 5-fluorouracil, and mitomycin-C.

III. Determine whether the increased response rate observed following hepatic arterial infusion of chemotherapy was a result of increased concentrations delivered to the tumor in the liver or is secondary to catheter placement and occlusion of the hepatic artery.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven colorectal carcinoma metastatic to the liver, without any evidence of extra-hepatic metastases, who have never received chemotherapy for liver metastases. Patients must have no greater than 70 percent liver involvement, and bilirubin must be less than or equal to 5.0 mg/dl. Patients with ascites will be excluded.

PROTOCOL OUTLINE: Nonrandomized study. Patients with multiple vessels supplying the liver will undergo hepatic arterial occlusion and enter Regimen A; patients with a single hepatic artery enter Regimen B.

Regimen A: 3-Drug Combination Intravenous Chemotherapy. Vindesine, DAVA, NSC-245467; Mitomycin-C, MITO-C, NSC-26980; 5-Fluorouracil, 5-FU, NSC-19893.

Regimen B: 3-Drug Combination Hepatic Arterial Infusion Chemotherapy. DAVA; MITO-C; Floxuridine, FUDR, NSC-27640.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests, hepatic function tests.

END POINTS: Response/remission rate, duration of response, survival.

CURRENT STATUS: 40-50 evaluable patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Hepatic arterial occlusion is performed and Chemotherapy initiated as soon as liver functions return to pre-infarction levels. DAVA - 3.0 mg/sqm continuous iv infusion over 12-24 hours on day 1; MITO-C - 10 mg/sqm iv infusion over 1 hour on day 2; 5-FU - 600 mg/sqm iv infusion over 4 hours daily for 5 days (5-FU is discontinued at the earliest sign of stomatitis).

Regimen B: DAVA - 3.0 mg/sqm continuous 24-hour hepatic arterial infusion (HAI) on day 1; MITO-C - 10 mg/sqm 2-hour HAI on day 2; FUDR - 100 mg/sqm continuous HAI on days 2 through 6. (FUDR should be discontinued at the first sign of mucositis; in the absence of mucositis, FUDR dose can be increased by increments of 25 percent in subsequent cycles.)

Treatment cycles are repeated every 28-35 days, or whenever safe.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

2.0096 PHASE II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR METASTATIC COLORECTAL CARCINOMA

Bedikian, A. Y., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-418; MDA-DT-8040

OBJECTIVES:

I. Determine the efficacy of anthracenedione administered on a five-day intravenous schedule to patients with metastatic colon cancer.

II. Determine the qualitative and quantitative toxicity of anthracenedione administered in this fashion.

III. Determine the duration of response and duration of survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of metastatic colorectal adenocarcinoma with measurable lesions who are not eligible for higher priority protocols. Patients must be at least 15 years of age and have a life expectancy of at least 12 weeks. Patients must have adequate bone marrow, liver, and renal function, unless this therapy is indicated as a life-saving measure. Patients must not receive any therapy for the 4 weeks prior to entry and must have recovered from the toxic effects of any previous therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Anthracenedione, Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Granulocyte and platelet counts.

END POINTS: Response/remission rate, duration of response, duration of survival, toxicity/morbidity of treatment.

CURRENT STATUS: At least 14 evaluable patients will be entered.

DOSAGE SCHEDULE:

DHAD - Good-risk patients receive 4 mg/sqm iv over 30 minutes daily for 5 days q 4 weeks; poor-risk patients receive 3 mg/sqm iv over 30 minutes daily for 5 days q 4 weeks. Chemotherapy is continued for a total of 2 years or for one year after achieving complete remission, whichever is shorter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

2.0097 CHEMOTHERAPY WITH MOF (MECCNU/VCR/5FU) VS MOF AND STREPTOZOTOCIN FOR METASTATIC COLORECTAL CARCINOMA

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PROTOCOL NUMBER(S) MSKCC-7867

OBJECTIVES:

I. Evaluate the effectiveness of MOF: methyl-CCNU (MeCCNU)/vincristine (VCR)/5-fluorouracil (5-FU) vs. MOF plus streptozotocin in patients with metastatic colorectal carcinoma and determine whether there is a significant improvement with MOF/SZC.

PROTOCOL ENTRY CRITERIA: Patients with measurable metastatic colon or rectal carcinoma previously untreated by chemotherapy and not rendered disease-free by radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. MOF: Methyl-CCNU, MeCCNU, NSC-95441; Vincristine, VCR, NSC-67574; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 4-Drug Combination Chemotherapy. MOF; Streptozotocin, SZC, NSC-85998.

STRATIFICATION BY: Karnofsky performance status: 60 or less vs. above 60; diagnosis to metastasis: 12 months or less vs. more than 12 months; lung involvement.

SPECIAL STUDY PARAMETERS: SMA-12, kidney function, CEA, liver scan.

END POINTS: Response rate, objective tumor response.

CURRENT STATUS: 128 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: MeCCNU - 35 mg/sqm po on days 1 through 5; 5-FU-350 mg/sqm iv days 1 through 5 and 36 through 40; VCR - 1 mg/sqm iv on day 1 and 36. Repeat courses q 72 days for 2 years.

Arm II: MeCCNU - 35 mg/sqm po days 2 through 6; 5-FU, VCR, as in Arm I; SZC - 500 mg/sqm (route not given) on day 1 and q 7 days. Repeat course q 71 days for 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/78

2.0098 SURGERY ALONE VS SURGERY PLUS RADIOTHERAPY FOR RECURRENT DUKES C COLORECTAL CARCINOMA

Sugarbaker, P. H., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America

PROTOCOL NUMBER(S) NCI-79-C-11

OBJECTIVES:

I. Evaluate and compare the sensitivity of 4 tests used serially to detect recurrent colorectal cancer: monthly serial symptom review and physical examination; monthly serial CEA assays; 3-monthly CAT scans; and 3-monthly abdominal ultrasound.

II. Test the efficacy of an adjuvant secondary local attack consisting of surgery plus radiation therapy on colorectal cancer after failure of standard surgical procedures.

III. Collect data concerning the biology of surgically treated colorectal cancer, e.g., the site of earliest recurrence and tendency to develop metastatic disease.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Dukes B2 or C colorectal cancer completely surgically resected within 3 months of entry, with no evidence of distant metastatic disease. The patient must be a candidate for possible resection of locally recurrent cancer. Patients may have received no prior adjunctive therapy, including chemotherapy, immunotherapy, and radiotherapy, for their primary colorectal cancer. Patients may not have concurrent serious medical problems or a history of malignant disease other than superficial skin cancer and basal cell carcinoma.

PROTOCOL OUTLINE: Randomized study. At the time of evidence of local recurrence without distant metastasis and if laparoscopy reveals histologic proof of local recurrence that can be completely resected, randomize patients to Arms I and II.

Arm I: Surgery.

Arm II: Surgery plus Radiotherapy. Linear accelerator.

STRATIFICATION BY: Site of primary tumor (colon vs. rectum).

SPECIAL STUDY PARAMETERS: Serial CEA, serial physical examination, serial CAT scan, serial ultrasound, SMA-21, hemogram, EKG, chest x-ray, full lung tomography, liver scintiscan, IVP, colonoscopy or barium enema, upper GI series.

END POINTS: Disease-free interval, survival, toxicity/morbidity of treatment.

CURRENT STATUS: About 66 patients per year will be entered for each of 3 years.

DOSAGE SCHEDULE:

Arm I: Extensive resection of tumor, with en-bloc resection of all tumor that does not involve a vital organ.

Arm II: Surgery as in Arm I. Radiotherapy - 5000-5500 rads to the tumor-bearing area over 7-8 weeks; 4500-5000 rads to areas of possible tumor infiltration over 607 weeks. Begin treatment as soon as possible after Surgery, using daily fractions of 170-180 rads.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 10/80

2.0099 INTRAVENOUS VS INTRAPERITONEAL 5-FU AS ADJUVANT CHEMOTHERAPY FOR DUKES C COLORECTAL CANCER

Sugarbaker, P. H., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-79-C-28

OBJECTIVES:

I. Compare disease-free interval and survival of Dules C colorectal cancer patients treated with iv vs. ip 5-fluorouracil as adjuvant chemotherapy.

II. Compare the morbidity of these 2 routes of 5-fluorouracil administration.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Dukes C colorectal cancer who have had complete surgical resection of tumor within 3 months of entry and who have no evidence of distant metastases. Patients must be candidates for possible resection of locally recurrent tumor. There must be no history of any prior chemotherapy, immunotherapy, or radiotherapy for the primary colorectal cancer, nor may there be complicating serious medical problems.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Intravenous 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Single-agent Chemotherapy. Intraperitoneal 5-FU.

STRATIFICATION BY: Site of primary tumor (colon vs. rectum), nodal involvement (1-4 positive nodes vs. 5 or more).

SPECIAL STUDY PARAMETERS: Serial monthly CEA, monthly serial physical examination, 3-monthly serial abdominal CAT scans, 3-monthly abdominal ultrasound, liver scan, chest x-ray, IVP, barium enema, colonoscopy, indocyanine green clearance.

END POINTS: 3-year disease-free interval, survival, sites of failure, morbidity of treatment.

CURRENT STATUS: 65 patients will be entered on each arm over 2 years.

DOSAGE SCHEDULE:

Arm I: 5-FU - 12 mg/kg/day iv over 1 hour for 5 consecutive days, beginning within 2 months of resection. Repeat monthly for a total of 12 courses. Escalate by 20 percent in subsequent cycles until mild toxicity is encountered.

Arm II: 5-FU - 820 mg in 2 liters of fluid introduced into the peritoneal cavity via a Tenckhoff catheter, daily for 5 consecutive days. Repeat monthly for a total of 12 courses. Escalate subsequent doses by increments of 100 mg until mild toxicity is encountered. Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

2.0100 EVALUATION OF PREOPERATIVE, ADJUVANT RADIOTHERAPY PRIOR TO SURGICAL RESECTION FOR RECTAL CARCINOMA

Higgins, G. A., (202-389-7266) Veterans Administration Surgical Oncology Group, 50 Irving St. N.W., Washington, District of Columbia, 20422, United States of America
PROTOCOL NUMBER(S) VASOG-28

OBJECTIVES:

I. Determine the efficacy of preoperative radiation in cancer of the rectum.

PROTOCOL ENTRY CRITERIA: Male patients with adenocarcinoma of the rectum who are candidates for potentially curative abdominoperineal resection.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery. Abdominoperineal resection alone.

Arm II: Radiotherapy plus Surgery. Supervoltage Radiotherapy; plus abdominoperineal resection.

STRATIFICATION BY: Extent of surgery (curative or palliative), and pathological classification of resected specimen (microscopically negative or positive).

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Relapse/recurrence rate; disease-free interval; survival rate; length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Standard abdominoperineal resection, unless there is frozen-section proof of residual disease. In those cases, a resection with anastomosis or a Hartmann procedure may be used.

Arm II: Abdominoperineal resection as in Arm I plus preoperative radiotherapy to the primary tumor and adjacent lymph node drainage area in the pelvis and extending along the superior hemorrhoidal vessels. The total tumor dosage will be 3150 rads in 24 days. Patients will undergo Surgery within 3 weeks following completion of Radiotherapy.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 12/76

2.0101 PHASE II CHEMOTHERAPY WITH AMSA FOR DISSEMINATED ADENOCARCINOMA OF THE COLON OR RECTUM

Baker, L. H., (313-494-6232) Wayne State University, United Hospitals of Detroit, 4160 John R St., Detroit, Michigan, 48235, United States of America
PROTOCOL NUMBER(S) WSU-C-27778

OBJECTIVES:

I. Determine the antitumor effect of AMSA in disseminated large bowel cancer.

II. Determine the nature and extent of toxicity of AMSA administered on an every three week schedule.

PROTOCOL ENTRY CRITERIA: Patients with measurable, biopsy-proven, incurable adenocarcinoma of the colon or rectum. Patients must have a performance status of 50% or better and a minimum life expectancy of 6 weeks. They must have passed the nadir of myelosuppression from prior therapy, and radiotherapy encompassing major bone marrow sites must have been completed 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions, previous treatment.

SPECIAL STUDY PARAMETERS: SMA-17, Coomb's test, haptoglobin.

END POINTS: Response/remission rate, duration of response, duration of survival, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 14 to 39 patients will be entered.

DOSAGE SCHEDULE:

AMSA - 75 mg/sqm iv on day 1. Repeat course q 3 weeks. Doses of 40 mg/sqm and 55 mg/sqm will be used to start very poor-risk and poor-risk patients, respectively. (Poor-risk: over 65 years old, wbc between 2,000 and 4,000, platelets between 100,000 and 75,000, prior extensive radiotherapy to more than 50% of marrow bearing areas, and/or prior intolerance to chemotherapy and moderately impaired liver function; very poor-risk: patients with severely impaired liver function.) Doses will be escalated if tolerated. Evaluate after 2 courses and remove from study patients with progressive disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 11/78

2.0102 PHASE II CHEMOTHERAPY WITH ICRF-187 FOR DISSEMINATED ADENOCARCINOMA OF THE COLON AND RECTUM

Leichman, L. P., (313-494-6433) Wayne State University, Dept. of Oncology, 3990 John R Street, Detroit, Michigan, 48201, United States of America
PROTOCOL NUMBER(S) WSU-C-36480

OBJECTIVES:

I. Determine the nature and extent of toxicity of ICRF-187 administered via a 48-hour infusion every three weeks.

II. Determine the antitumor effect of ICRF-187 in disseminated large bowel cancer.

III. Determine whether changes in the carcinoembryonic antigen (CEA) level correlate with changes in measurable disease parameters in patients treated with ICRF-187.

PROTOCOL ENTRY CRITERIA: Patients of all ages with biopsy-proven incurable adenocarcinoma of the colon or rectum. The disease must be clearly measurable. There can be no renal impairment; BUN should be 20 mg percent or less and creatinine 1.5 mg percent or less. Impaired liver function is acceptable; bilirubin should be 2 mg percent or less. Expected survival should be at least 6 weeks, and the performance status should be at least 50 percent (Karnofsky). Patients must have passed the nadir of myelosuppression from prior chemotherapy. Prior radiotherapy to a major bone marrow site must be completed at least 3 weeks before entry. The carcinoembryonic antigen level must be determined before therapy begins.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. ICRF-187, NSC-169780.

STRATIFICATION BY: Prognostic risk.

SPECIAL STUDY PARAMETERS: CBC, platelets, CEA, liver function.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, duration of response, recurrence rate, length of survival.

CURRENT STATUS: 14-25 patients will be entered.

DOSAGE SCHEDULE:

ICRF-187 - 1000 mg/sqm (750 mg/sqm in poor-risk patients) iv infusion over 48 hours. Repeat q 3 weeks. Poor-risk patients are more than 65 years of age, with prior extensive Radiotherapy to 50 percent or more of marrow-bearing areas, liver enzymes greater than twice normal, or previously treated with nitrosoureas or Mitomycin-C. Two full 3-week courses are required for adequate evaluation.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ICRF-187 - 250 mg vials.

DATE SUMMARIZED: 10/80

2.0103 PHASE II CHEMOTHERAPY WITH PCNU FOR DISSEMINATED ADENOCARCINOMA OF THE COLON AND RECTUM

Leichman, L. P., (313-494-6433) Wayne State University, Dept. of Oncology, 3990 John R Street, Detroit, Michigan, 48201, United States of America
PROTOCOL NUMBER(S) WSU-C-36580

OBJECTIVES:

I. Determine the antitumor effect of PCNU in disseminated large bowel cancer.

II. Determine the nature and extent of toxicity of PCNU administered every 6 weeks.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven incurable adenocarcinoma of the colon and rectum, with clearly measurable disease, who are not candidates for a higher priority protocol. Patients must have a life expectancy of at least 6 weeks and a Karnofsky performance status of at least 50 percent. Patients with liver/renal dysfunctions greater than 2 times normal laboratory values will be eligible after discussion with investigator. Patients must have recovered from the toxic effects of any prior chemotherapy. Previous treatment with other nitrosoureas is not allowed. Radiotherapy is permitted to areas other than measurable tumor, but radiotherapy encompassing a major bone marrow site must be completed at least 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PCNU, NSC-95466.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurement, CBC, platelets, CEA, urinalysis, BUN, creatinine, SMA-17, ECG, liver function studies, bone marrow.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment, duration of survival.

CURRENT STATUS: Initially, 14 patients will be treated. If there is at least one response among these 14 patients, the study will be extended to 25 patients.

DOSAGE SCHEDULE:

PCNU - 100 mg/sqm iv infusion over one hour through a free-running iv. Poor-risk patients (over 65 years old, extensive prior radiation to 50 percent or more of marrow-bearing areas, liver enzymes greater than 2 times normal) receive 75 mg/sqm on the same schedule. One course of therapy is defined as one dose of PCNU followed by 5 weeks rest. Patients will be evaluable for response if at least one course of therapy was given.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PCNU - 50 mg vials.

DATE SUMMARIZED: 11/80

2.0104 CHEMOTHERAPY WITH 5-FU OR IMMUNOTHERAPY WITH AUTOLOGOUS TUMOR CELLS FOR RESECTED COLORECTAL ADENOCARCINOMA

Elias, E. G., (301-528-5835) University of Maryland, Dept. of Surgery, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) MD-CO-1

OBJECTIVES:

I. Prolong disease-free interval and improve length of survival by chemotherapy with 5-FU or immunotherapy with autologous tumor cells in patients who have undergone curative resection and were found to have Dukes B2, C1, or C2 adenocarcinoma of the colon or rectum.

PROTOCOL ENTRY CRITERIA: Patients between the ages of 30 and 80 years who have undergone curative resection of colorectal carcinoma. Patients should have Dukes B2 or C disease, have recovered completely from surgery, and be taking a regular diet. Patients with Dukes A or B1 disease will receive no further therapy but will be placed under observation.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Immunotherapy. Autologous tumor cells; Freund's complete adjuvant, FCA, no NSC number.

STRATIFICATION BY: Age; sex; tumor site, stage, and size; number of positive lymph nodes.

SPECIAL STUDY PARAMETERS: CEA, leukocyte migration inhibition assay, indirect ELISA for antibody, helper and suppressor cells, and serum glycoprotein.

END POINTS: Recurrence rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: 5-FU - 400 mg/sqm iv daily for 5 days. Repeat q 6 weeks for 8 courses.

Arm II: Autologous tumor cells in FCA - 200 x 10 to the sixth id q 4 weeks. Repeat for 3 courses.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 07/80

2.0105 IMMUNOTHERAPY WITH BCG AND CHEMOTHERAPY WITH 5-FU/MECCNU ALONE AND COMBINED FOR DISSEMINATED COLON CANCER

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PROTOCOL NUMBER(S) MI-CO-1

OBJECTIVES:

I. Determine whether immunotherapy with Tice-BCG (BCG) alone or in combination with chemotherapy using 5-fluorouracil (5-FU) plus methyl-CCNU (MeCCNU) or chemotherapy alone is more effective in improving the survival time of patients with known disseminated adenocarcinoma of the colon.

PROTOCOL ENTRY CRITERIA: Patients with primary adenocarcinoma of the colon with residual tumor after surgery or evidence of metastases in liver scan or chest x-ray.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: 2-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Methyl-CCNU, MeCCNU, NSC-95441.

Arm III: 2-Drug Combination Chemotherapy plus Immunotherapy. 5-FU; MeCCNU; plus BCG.

Arm IV: No further treatment.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be admitted.

DOSAGE SCHEDULE:

Arm I: BCG - 1 ampule/week for 3 weeks, divided between both axillae and both groin areas, and given by multiple puncture tine technique. Following this, BCG by alternate multipuncture and oral doses weekly for 12 weeks, then every other week for 2 years.

Arm II: Phase A: 5-FU - 325 mg/sqm iv on days 1 through 5; MeCCNU - 130 mg/sqm po on day 1. Phase B: 5-FU - 375 mg/sqm iv on days 36 through 46. Phases A and B are alternated every 35 days (5 weeks); a complete cycle lasts 10 weeks.

Arm III: BCG; 5-FU; MeCCNU as in Arms I and II.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - ampule containing 2-8 x 10 to the eighth CFU.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

2.0106 IMMUNOTHERAPY WITH BCG AND COMBINATION CHEMOTHERAPY WITH 5-FU/MECCNU IN ADJUVANT TREATMENT OF COLON CANCER

Kerry, R. L., (313-973-2800) St. Joseph's Mercy Hospital, P.O. Box 995, Ann Arbor, Michigan, 48106, United States of America
PROTOCOL NUMBER(S) MI-CO-2

OBJECTIVES:

I. Determine whether adjuvant immunotherapy with BCG-Tice (BCG) or adjuvant chemotherapy with 5-fluorouracil (5-FU) plus methyl-CCNU (MeCCNU) or the combination of these therapies will improve the cure rate of colon cancer when added to potentially curative surgery.

PROTOCOL ENTRY CRITERIA: Patients with adenocarcinoma of the colon in whom all detectable tumor has been surgically excised. Spread to local lymph nodes or serosal penetration must be documented.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: 2-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Methyl-CCNU, MeCCNU, NSC-95441.

Arm III: 2-Drug Combination Chemotherapy plus Immunotherapy. 5-FU; MeCCNU; plus BCG.

Arm IV: No further treatment.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be admitted.

DOSAGE SCHEDULE:

Arm I: BCG - 1 ampule/week for 3 weeks, divided between both axillae and both groin areas and given by multiple-puncture tine technique. Following this, BCG by alternate multipuncture and oral doses weekly for 12 weeks, then every other week for 2 years.

Arm II: Phase A: 5-FU - 325 mg/sqm iv on days 1 through 5; MeCCNU - 130 mg/sqm po on day 1. Phase B: 5-FU - 375 mg/sqm iv on days 36 through 46. Phases A and B are alternated every 35 days (5 weeks); a complete cycle lasts 10 weeks.

Arm III: BCG; 5-FU; MeCCNU. All as in Arms I and II.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - ampule containing 2-8 x 10 to the eighth CFU.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

2.0107 ADJUVANT IMMUNOTHERAPY WITH BCG IN COLORECTAL CARCINOMA

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PROTOCOL NUMBER(S) MI-CRC-113628D

OBJECTIVES:

I. Determine the efficacy of nonspecific immunotherapy with BCG in prolonging the disease-free interval and survival of patients with Dukes B colorectal carcinoma after curative surgical excision of their lesions.

II. Compare two routes of administration of BCG immunotherapy, namely orally and by scarification, as to their effectiveness and side effects.

PROTOCOL ENTRY CRITERIA: Patients with Dukes B adenocarcinoma of the colon and rectum (no mesenteric nodal extension, no metastasis) who have undergone curative surgical resection.

PROTOCOL OUTLINE: Randomized study.

Arm I: No further therapy.

Arm II: Single-agent Immunotherapy. BCG (Connaught Strain), BCG, NSC-B116341, po.

Arm III: Single-agent Immunotherapy. BCG, by scarification.

STRATIFICATION BY: Age (70 years or younger), sex, site (disease in the abdominal colon or rectum).

SPECIAL STUDY PARAMETERS: Immunocompetent status; total lymphocyte count, preoperatively; skin tests for recall antigens (Mumps, Varidase, SK-SK).

END POINTS: Length of disease-free interval and length of survival.

CURRENT STATUS: 50-60 patients will be entered.

DOSAGE SCHEDULE:

Arm I: No further therapy.

Arm II: BCG - 120 mg or 1.9 x 10 to the ninth viable organisms (3 vials), po.

Arm III: BCG - same dosage as in Arm II, by scarification.

Treatment begins 14-21 days postoperatively and is repeated weekly for 3 months, then bi-weekly for 3 months, then monthly for the last 6 months of the treatment year or until disease recurrence or death.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - vials containing 4 x 10 to the eighth to 1.2 x 10 to the ninth CFU.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

2.0108 IMMUNOTHERAPY WITH VACCINIA ONCOLYSATE AND CHEMOTHERAPY WITH 5-FU ALONE AND COMBINED FOR CARCINOMA OF THE COLON

Wallack, M. K., (314-454-2919) Washington University School of Medicine, Department of Surgery, 4960 Audubon Avenue, St. Louis, Missouri, 63110, United States of America
PROTOCOL NUMBER(S) MO-CO-1

OBJECTIVES:

I. Evaluate the ability of a live vaccinia virus-lysed autochthonous or allogeneic tumor cell vaccine to extend disease-free interval in Dukes B, C, and D colon cancer.

II. Determine the effect of repeated vaccinia oncolysate injections on both in vitro and in vivo immune function.

PROTOCOL ENTRY CRITERIA: Patients with Dukes B, C, and D adenocarcinoma of the colon with no residual tumor or minimal to moderate residual tumor following surgery. No prior chemotherapy, immunotherapy or radiation therapy is allowed. Patients must not be anergic.

PROTOCOL OUTLINE: Randomized study. Dukes B and C to Arms I, II; Dukes D to Arms III, IV.

Arm I: No therapy.

Arm II: Immunotherapy. Vaccinia oncolysate.

Arm III: Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Arm IV: Single-agent Chemotherapy plus Immunotherapy. 5-FU; Vaccinia oncolysate.

STRATIFICATION BY: Sex, Dukes classification, time lapse since surgery, location and number of lesions, immunoreactivity.

SPECIAL STUDY PARAMETERS: Follow-up of CEA, 12, CXR, liver and bone scans, barium enema, and proctoscopy.

END POINTS: Survival time, disease-free interval.

CURRENT STATUS: 30 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm II: Vaccinia oncolysate - 2 ml id in 4 divided doses on week one, then 1 ml weekly for 12 weeks, then every other week for 18 months.

Arm III: 5-FU - 12 mg/kg iv daily for 5 days then weekly for 4 weeks; if no toxicity, dose increased to 15 mg/kg, weekly for 18 months.

Arm IV: 5-FU as in Arm III; Vaccinia oncolysate as in Arm II.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Vaccinia oncolysate - 1 ml ampules; 5-FU - 500 mg vials.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

2.0109 IMMUNOTHERAPY WITH VACCINIA ONCOLYSATE AND CHEMOTHERAPY WITH 5-FU, ALONE AND IN COMBINATION FOR CARCINOMA OF RECTUM

Wallack, M. K., (314-454-2919) Washington University School of Medicine, Department of Surgery, 4960 Audubon Ave., St. Louis, Missouri, 63110, United States of America
PROTOCOL NUMBER(S) MO-GI-1

OBJECTIVES:

I. Evaluate the ability of a live vaccinia virus-lysed autochthonous or allogenic tumor cell vaccine to extend disease-free interval in Dukes B, C, and D rectal cancer.

II. Determine the effect of repeated vaccinia oncolysate injections on both in vitro and in vivo immune function.

PROTOCOL ENTRY CRITERIA: Patients with Dukes B, C, and D adenocarcinoma of the rectum with no residual tumor or minimal to moderate residual tumor following operation. Patients must not be anergic, and may not have received any previous chemo- or immunotherapy; they may have had pre-operative radiation therapy.

PROTOCOL OUTLINE: Nonrandomized study. Assign patients with Dukes B and C to Regimens A and B, patients with Dukes D to Regimens C and D.

Regimen A: No therapy.

Regimen B: Immunotherapy. Vaccinia oncolysate.

Regimen C: Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Regimen D: Single-agent Chemotherapy plus Immunotherapy. 5-Fluorouracil plus Vaccinia oncolysate.

STRATIFICATION BY: Sex, Dukes classification, time lapse since surgery, location and number of lesions, immunoreactivity, previous radiotherapy (or not).

SPECIAL STUDY PARAMETERS: Follow-up of CEA, 12, CXR, liver and bone scans, barium enema, and proctoscopy.

END POINTS: Survival time, disease-free interval.

CURRENT STATUS: 30 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Regimen A: No treatment.

Regimen B: Vaccinia oncolysate - 2 cc id in 4 divided doses week 1, then 1 cc weekly for 12 weeks, then alternate weeks for 18 months.

Regimen C: 5-FU - 12 mg/kg iv daily for 5 days, then weekly for 4 weeks. Dosage increased to 15 mg/kg if no toxicity, then weekly for 18 months.

Regimen D: Vaccinia oncolysate as in Regimen B; plus 5-FU as in Regimen C; 5-FU to begin on week 3 after start of Vaccinia oncolysate.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Vaccinia oncolysate - 1 cc ampules; 5-FU - 500 mg vials.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

2.0110 PHASE II-III THERAPY WITH 5-FU VS 5-FU/TZT VS 5-FU/ICRF-159 VS MECCNU/ICRF-159 VS MECCNU/TZT VS ICRF-159/TZT FOR ADVANCED COLORECTAL CANCER

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PROTOCOL NUMBER(S) NCCTG-784651

OBJECTIVES:

I. Compare 5-fluorouracil (5-FU) alone vs. 5-FU/Baker's antifol (TZT) vs. 5-FU/ICRF-159 vs. methyl CCNU (MeCCNU)/ICRF-159 vs. MeCCNU/TZT vs. ICRF-159/TZT in the treatment of advanced colorectal carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically or cytologically confirmed, unresectable or metastatic colorectal cancer with a confirmed primary lesion in the large bowel which is not amenable to more conventional treatment. Patients must be ambulatory with performance status better than 4 and adequate renal, hepatic, bone marrow function and nutritional status. Patients must not have symptomatic cerebral vascular disease or convulsive disorders. Previous nitrosourea therapy must be completed by 7 weeks prior to entry, other cytotoxic or radiotherapy by 4 weeks.

PROTOCOL OUTLINE: Randomize patients without prior Chemotherapy to Arm I, II, III, IV, V or VI and cross over nonresponders as indicated. Randomize patients with prior 5-FU therapy to Arm IV, V or VI; randomize patients with prior MeCCNU therapy to Arm II, III or VI; randomize patients with prior TZT therapy to Arm III or IV; randomize patients with prior ICRF-159 therapy to Arm II or V.

Arm I: Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 2-Drug Combination Chemotherapy. 5-FU, Baker's Antifol, TZT, NSC-139105.

Arm III: 2-Drug Combination Chemotherapy. 5-FU, ICRF-159, NSC-129943.

Arm IV: 2-Drug Combination Chemotherapy. ICRF-159, Methyl CCNU, MeCCNU, NSC-95441.

Arm V: 2-Drug Combination Chemotherapy. MeCCNU, TZT.

Arm VI: 2-Drug Combination Chemotherapy. ICRF-159; TZT.

STRATIFICATION BY: Participating institutions; prior radiation or chemotherapy; performance status: 0 and 1 vs. 2 and 3; site of primary indicator lesion: hepatic vs. pulmonary vs. other.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, response rate, duration of response, interval to progression, survival.

CURRENT STATUS: 180 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: 5-FU - 500 mg/sqm iv on days 1 through 5 q weeks or until disease progression. Cross over to Arm VI any patients without prior Chemotherapy.

Arm II: 5-FU - 400 mg/sqm iv on days 1 through 5; TZT - 175 mg/sqm iv on days 1 through 3. Repeat course q 5 weeks or until disease progression. Cross over to Arm IV patients without prior Chemotherapy.

Arm III: 5-FU - as in Arm II; ICRF-159 - 600 mg/sqm iv on days 1 through 3. Repeat course q 5 weeks or until disease progression. Cross over to Arm V patients without prior Chemotherapy.

Arm IV: MeCCNU - 150 mg/sqm po on day 1, ICRF-159 - 600 mg/sqm po on days 2 through 4 and 29 through 31. Repeat course q 8 weeks or until disease progression. Cross over to Arm II patients without prior Chemotherapy.

Arm V: MeCCNU as in Arm IV; TZT - 200 mg/sqm iv on days 1 through 3 and 29 through 31. Repeat course q 8 weeks or until disease progression. Cross over to Arm III patients without prior Chemotherapy.

Arm VI: ICRF-159 - 425 mg/sqm po on days 1 through 3; TZT - 125 mg/sqm iv on days 1 through 3. Repeat course q 4 weeks or until disease progression. Cross over to Arm I patients without prior Chemotherapy.

Remove all patients with prior Chemotherapy with study agents from study at progression. Cross over patients with no prior Chemotherapy with study agents to another arm as indicated. Remove from study if progression occurs on crossover therapy. Follow up all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg vials; MeCCNU - 10, 20, 50 and 100 mg capsules; ICRF-159 - 50, 250 and 500 mg tablets; TZT - 100 and 250 mg vials.

DATE SUMMARIZED: 11/78

2.0111 ADJUVANT LEVAMISOLE IMMUNOTHERAPY WITH VS WITHOUT 5-FLUOROURACIL FOR SURGICALLY CURED COLORECTAL CARCINOMA

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PROTOCOL NUMBER(S) NCCTG-784852

OBJECTIVES:

I. Compare the effectiveness of levamisole with and without 5-fluorouracil as surgical adjuvants for resectable colorectal carcinoma when compared to untreated controls.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven, curatively resected adenocarcinoma of the colon or rectum without gross or microscopic evidence of residual disease. Patient must present poor prognosis as indicated by resected specimen with modified Dukes Stages B2, B3 or C. Patients must be free of distant metastases and regional metastasis unresectable en bloc with primary. Patients must not have had previous 5-FU therapy or radiotherapy to the lumbar spine or pelvis, and must have adequate hematologic status.

PROTOCOL OUTLINE: Randomized study. Patients are randomized following Surgery.

Arm I: No adjuvant therapy.

Arm II: Immunotherapy. Levamisole, LEV, NSC-177023.

Arm III: Single-agent Chemotherapy plus Immunotherapy. LEV; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Participating institutions; location of disease: cecum, ascending, transverse colon, vs. descending, sigmoid colon and peritoneal reflection, vs. rectum below peritoneal reflection; Dukes classification (NCCTG modification): B2, B3 vs. C1 (A), C1 (B1) vs. C1 (B2), C1 (B3), vs. C2 (A), C2 (B1), C2 (B2), C2 (B3).

SPECIAL STUDY PARAMETERS: Hepatic and renal function, proctoscopy, liver scan, colon x-ray.

END POINTS: Survival rate, interval to recurrence, recurrence rate, length of survival.

CURRENT STATUS: 400 eligible patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: No treatment. Follow patients for 5 years or until disease progression.

Arm II: Begin within 4 weeks following Surgery, when patients can reliably take oral medication. LEV - 50 mg po q 8 hours on days 1 through 3. Repeat course q 14 days for 1 year or until progression.

Arm III: Begin within 21 to 28 days following Surgery, when surgical recovery is complete. LEV as in Arm II; 5-FU - 450 mg/sqm iv on days 1 through 5, and beginning on day 28 q week for 1 year or until progression.

Continue therapy for 12 months or until recurrence. Observe all patients for 5 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: LEV - 50 mg tablets; 5-FU - 500 mg vials.

DATE SUMMARIZED: 10/78

2.0112 POSTOPERATIVE RADIOTHERAPY ALONE VS POSTOPERATIVE MECCNU/5-FU SEQUENTIAL CHEMOTHERAPY PLUS RADIOTHERAPY FOR RECTAL CARCINOMA

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PROTOCOL NUMBER(S) NCCTG-794751; MAYO-794751

OBJECTIVES:

I. Compare local recurrence rates, rates of distant metastasis, recurrence-free survival, and overall survival in patients having potentially curative resections of Dukes B2 and C rectal carcinoma treated either with postoperative radiation alone or with sequential chemotherapy using methyl-CCNU and 5-fluorouracil plus postoperative radiation.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven Dukes B2 or C adenocarcinoma of the rectum in whom a potentially curative resection has been performed with neither gross nor microscopic evidence of residual disease. There may have been no prior chemotherapy nor radiotherapy to the pelvis. Bone marrow function must be adequate and the patient must have recovered from the acute effects of surgery and be maintaining normal oral nutrition. There may be no history of any malignant disease within the previous 5 years other than squamous or basal cell carcinoma of the skin or in situ carcinoma of the cervix.

PROTOCOL OUTLINE: Randomized study. After stratification, randomize patients to Arms I and II.

Arm I: Radiotherapy. Supervoltage therapy using Co-60 or linear accelerator.

Arm II: Radiotherapy plus 2-Drug Combination Chemotherapy. Methyl-CCNU, MeCCNU, NSC-95441; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Participating institutions, type of surgery (abdominal perineal resection vs. anterior resection), Dukes classification (B2 vs. C1 vs. C2), interval between surgery and randomization (21-35 days vs. 36-56 days).

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, chest x-ray, proctoscopy, colon x-ray.

END POINTS: Local recurrence rates, rates of distant metastasis, recurrence-free survival, survival.

CURRENT STATUS: 200 patients will be accrued.

DOSAGE SCHEDULE:

Arm I: 4500 rads over 5 weeks in 5 daily fractions per week of 180 rads, beginning 21-56 days postoperatively.

Arm II: MeCCNU - 130 mg/sqm po on day 1; 5-FU - 350 mg/sqm iv on days 1 through 5; 5-FU - 400 mg/sqm iv on days 36 through 40. Radiotherapy to begin on day 63 with additional 5-FU - 500 mg/sqm day iv on the first 3 and last 3 days of Radiotherapy. Beginning 28 days after completion of Radiotherapy: MeCCNU - 100 mg/sqm po on day 1; 5-FU - 300 mg/sqm iv on days 1 through 5 and 400 mg/sqm iv on days 36-40. Continue follow-up for a minimum of 5 years. If histologic evidence of recurrence is obtained, enter patient on protocol for advanced colorectal cancer.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg vials; MeCCNU - 10, 20, 50, and 100 mg capsules.

DATE SUMMARIZED: 08/80

2.0113 PHASE III CHEMOTHERAPY WITH VCR/MECCNU/5-FU FOR CARCINOMA OF THE COLON IN CHILDREN

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PROTOCOL NUMBER(S) SJCRH-GIC-1

OBJECTIVES:

I. Provide optimal chemotherapy with vincristine (VCR)/methyl-CCNU (MeCCNU)/5-fluorouracil (5-FU) for pediatric patients with colon carcinoma.

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age with measurable carcinoma of the colon. Patients must have adequate renal function and must not have had prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study. 3-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Methyl-CCNU, MeCCNU, NSC-95441; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: CEA, dietary history, bone and liver scan, IVP, upper GI series, barium enema.

END POINTS: Response/remission rate, objective tumor response, quality and duration of response, toxicity/morbidity of treatment, survival time, disease-free interval.

CURRENT STATUS: 1-2 patients per year are expected to be entered.

DOSAGE SCHEDULE:

VCR - 1.5 mg/sqm iv started at 6 pm on days 1, 8, and 15; MeCCNU - 100 mg/sqm po started at 6 pm on day 2; 5-FU - 200 mg/sqm po (increase to 250 mg/sqm in Course 3 if tolerated) at 6 pm and 12 pm on day 2, and on days 3 through 6 give 4 doses/day q 6 hours plus 2 doses on day 7 for a total of 20 doses. Repeat course q month for 18 months or until progressive disease. Follow all patients for recurrence, toxicity and survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

2.0114 CHEMOTHERAPY WITH 5-FU/VCR/MECCNU WITH AND WITHOUT IMMUNOTHERAPY WITH C. PARVUM IN ADVANCED COLORECTAL CANCER

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Oncology Unit, Fitzroy, Victoria 3065, Australia

PROTOCOL NUMBER(S) AUS-CO-1

OBJECTIVES:

I. Evaluate the efficacy and toxicity of 3-drug combination chemotherapy with 5-fluorouracil, vincristine, and methyl-CCNU in advanced colorectal cancer.

II. Evaluate the efficacy and toxicity of the addition of immunotherapy with C. parvum to the chemotherapy regimen.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven, advanced or metastatic adenocarcinoma of the colon.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Vincristine, VCR, NSC-67574; Methyl-CCNU, MeCCNU, NSC-95441.

Arm II: 3-Drug Combination Chemotherapy plus Immunotherapy. 5-FU; VCR; MeCCNU; plus Corynebacterium parvum (unspecified), C. parvum.

STRATIFICATION BY: Liver metastases vs. no liver metastases.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Progressive disease, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: 5-FU - 1.5 gm/sqm iv q 4 weeks; VCR - 1 mg iv q 4 weeks; MeCCNU - 130 mg/sqm po q 8 weeks.

Arm II: 5-FU, VCR, MeCCNU, all as in Arm I. C. parvum - 2.5 mg/sqm iv on days 14 and 21 of each 28-day course.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: MeCCNU - 20, 50, and 100 mg capsules.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

2.0115 ADJUVANT IMMUNOTHERAPY WITH BCG PLUS NEURAMINIDASE-TREATED CELLS FOR OPERABLE COLORECTAL CANCER

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Fitzroy, Victoria 3065, Australia

PROTOCOL NUMBER(S) AUS-CO-2

OBJECTIVES:

I. Determine whether the disease-free interval and ultimate survival can be prolonged in patients with operable colorectal cancer by administration of neuraminidase-treated cancer cells (NTT) plus BCG (unspecified).

PROTOCOL ENTRY CRITERIA: Patients less than 80 years of age with Dukes Stages B and C colorectal cancer. Patients must have had no other malignancies during the previous 5 years.

PROTOCOL OUTLINE: Randomized study. All patients undergo initial surgery.

Arm I: No post-resection treatment.

Arm II: Immunotherapy. BCG, unspecified; plus neuraminidase-treated autologous tumor cells, NTT.

STRATIFICATION BY: Disease stage.

SPECIAL STUDY PARAMETERS: 3-month follow-up for 5-year period.

END POINTS: Disease recurrence rate, length of survival.

CURRENT STATUS: 107 patients have been entered as of March, 1980.

DOSAGE SCHEDULE:

Arm I: Control, no treatment.

Arm II: NTT - 0.5 x 10 to the sixth, s.c, 18 vaccinations over 2-year period; BCG - 60 mg, by scarifications over 2-year period.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

2.0116 IMMUNOTHERAPY WITH LEV WITH OR WITHOUT CHEMOTHERAPY WITH 5-FU ADJUVANT TO SURGERY FOR CARCINOMA OF THE COLON AND RECTUM

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PROTOCOL NUMBER(S) CAN-NCIC-CO-1

OBJECTIVES:

I. Determine the usefulness of giving levamisole alone and continuing it for 2 years in preventing recurrence and increasing survival of patients with apparently curative resection of Dukes B2 and C colon and rectal cancer above the peritoneal reflection.

II. Determine whether the addition of adjuvant chemotherapy with 5-fluorouracil improves the effectiveness of levamisole in preventing recurrence and increasing survival of patients with apparently curative resection of Dukes C colon and rectal carcinoma above the peritoneal reflection.

PROTOCOL ENTRY CRITERIA: Patients with Dukes Stage B2 or C carcinoma of the colon or rectum above the peritoneal reflection with an en bloc curative resection. Patients must not have isolated, distant intra-abdominal metastases, even if apparently resected, or have received preoperative irradiation to the tumor area, or any form of chemotherapy or immunotherapy.

PROTOCOL OUTLINE: Randomized study. Patients with Dukes Stage B2 carcinoma are randomized to Arms I and III, those with Dukes Stage C carcinoma to Arms I, II, and III. Patients are randomized following surgery.

Arm I: Immunotherapy. Levamisole, LEV, NSC-177023.

Arm II: Single-agent Chemotherapy plus Immunotherapy. LEV; plus 5-Fluorouracil, 5-FU, NSC-19893.

Arm III: No further treatment.

STRATIFICATION BY: Colon and rectum by Dukes Stage: B2 or C.

SPECIAL STUDY PARAMETERS: Skin test with Connaught PPD, 5-TU with Tween 80, and varidase; CEA; hematologic, renal and hepatic function tests.

END POINTS: Survival rate, length of survival, disease-free interval, quality of survival, rate of recurrence.

CURRENT STATUS: 26 patients are entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: LEV - 2.5 mg/kg po daily for 3 days beginning on days 1 and 15 of each 5-week cycle.

Arm II: LEV - 2.5 mg/kg po daily for 3 days beginning on days 1 and 15 of each 5-week cycle; plus 5-FU - 450 mg/sqm iv bolus on days 22 to 26 of each 5-week cycle.

Arm III: Observation only.

Treatment should begin no earlier than 21 days, but preferably within 6 weeks, following surgery. Patients continue on study until a definite recurrence of disease or until they have completed 2 years of treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: LEV - 2.5 mg capsules; 5-FU - 450 mg ampules.

DATE SUMMARIZED: 10/80

2.0117 SURGERY WITH AND WITHOUT PREOPERATIVE RADIOTHERAPY FOR LOCALIZED ADENOCARCINOMA OF THE RECTUM

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PROTOCOL NUMBER(S) EORTC-40761-PR1A; UICC-75034

OBJECTIVES:

I. Compare radical surgery alone vs. radical surgery preceded by radiotherapy for adenocarcinoma T2, T3 or T4 located in the last 15 cm of the rectum. This EORTC Protocol No. 40761 PR1a replaces the PR1 trial of Protocol No. 40741.

PROTOCOL ENTRY CRITERIA: Patients previously untreated except for colostomy or exploratory laparotomy with adenocarcinoma of the rectum localized to within 15 cm of the anal margin, without apparent distant metastases. The tumor must be clinically classified as potentially operable - T2, T3 or T4 and Nx, Mo.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radical Surgery.

Arm II: Radiotherapy - megavoltage: betatron or linear accelerator - to tumor prior to radical surgery.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum electrolytes, LHD levels, glucose tolerance, CEA, IVP, liver and bone scans, skeletal survey, LFT.

END POINTS: Toxicity/morbidity of treatment, survival rate, duration of survival, recurrence rate, disease-free interval, rate and time to appearance of metastases. Percent of invaded lymph nodes during surgery.

CURRENT STATUS: 152 patients will be entered in about 1 year.

DOSAGE SCHEDULE:

Arm I: Radical Surgery: Complete removal of the mesentery with the cancer-bearing bowel segment and complete removal of lymphatic drainage.

Arm II: Radiotherapy: 3450 rads given in 15 fractions over a period of 18 days to the tumor. Surgery: within 2 weeks of conclusion of radiotherapy perform radical surgery, as in Arm I. Follow up all patients q month for the first 3 months, q 3 months until the end of the second year, q 6 months in the third year and yearly until the end of the fifth year.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 01/77

2.0118 POSTOPERATIVE ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE FOR DUKES C RESECTABLE ADENOCARCINOMA OF THE COLON

Martin, F., (Dijon 80.652323) European Org. for Research on Treatment of Cancer, Gastrointestinal Tract Cooperative Group, Laboratoire d'Immunologie, 7 Blvd. Jeanne d'Arc, 21033 Dijon Cedex, France
PROTOCOL NUMBER(S) EORTC-40781

OBJECTIVES:

I. Compare, in a two-arm, prospective, double-blind, randomized trial which includes a placebo control, the efficacy of an adjuvant treatment with levamisole with respect to: (a) overall survival, (b) tumor-free interval.

PROTOCOL ENTRY CRITERIA: Patients who have had curative surgery without known residual disease of adenocarcinoma of the colon with lymphnode involvement. Patients must not have had previous therapy nor any other cancer except basal cell carcinoma of the skin, nor evidence of distant metastases. Patients must have adequate hematological and renal function.

PROTOCOL OUTLINE: Randomized double-blind study. Randomize patients within 7 days of surgery.

Arm I: Single-agent Immunotherapy. Levamisole, LEV, NSC-177023.

Arm II: Placebo.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Kidney function tests, CEA, liver scan.

END POINTS: Recurrence rate, length of survival, disease-free interval.

CURRENT STATUS: A total of 152 evaluable patients followed up until relapse is required. An entry rate of 75 eligible patients per year is anticipated.

DOSAGE SCHEDULE:

Begin treatment as soon as possible and preferably within 7 days following surgery.

Arm I: LEV - 100 mg for 50 kg or less body weight, 150 mg for 51 to 70 kg, 200 mg for 71 to 90 kg, given in 2 or 3 po doses on days 1 and 2 (the same two consecutive days of each week) for one year or until prior relapse or unacceptable toxicity. Adjust dosage to weight of patient during treatment.

Arm II: Placebo - same dosage as Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: LEV - 50 mg tablets.

DATE SUMMARIZED: 05/79

2.0119 RADIOTHERAPY PLUS 5-FU CHEMOTHERAPY WITH OR WITHOUT IMMUNOTHERAPY FOR COLORECTAL CANCER

Robinson, E., Israel Institute of Technology, RAMBAM Medical Center, Dept. of Oncology and Nuclear Medicine, Haifa, Israel
PROTOCOL NUMBER(S) ISR-CRC-1

OBJECTIVES:

I. Determine the effect of localized radiotherapy plus chemotherapy with 5-fluorouracil (5-FU) compared with the same treatment plus MER-BCG (MER) on the survival and disease-free interval of patients with colorectal cancer.

PROTOCOL ENTRY CRITERIA: Patients below the age of 70 with colorectal cancer, Stages B2 and C, after radical surgery.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus Single-agent Chemotherapy. Localized supervoltage irradiation; plus 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Radiotherapy plus Single-agent Chemotherapy plus Immunotherapy. Supervoltage; plus 5-FU; plus MER-BCG, MER, NSC-143769.

STRATIFICATION BY: Age, sex, disease stage.

SPECIAL STUDY PARAMETERS: Skin tests for 5 recall antigens, lymphocyte cultures, suppression cell activity.

END POINTS: Disease-free interval, length of survival.

CURRENT STATUS: 40 patients will be entered.

DOSAGE SCHEDULE:

Arm I: 4000 rads over 4 weeks, by two opposing fields. 5-FU - 13.5 mg/kg in 5 days q 4-5 weeks.

Arm II: 4000 rads plus 5-FU as in Arm I; plus MER (dosage dependent upon individual skin sensitivity), given 2 weeks after each 5-FU treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

2.0120 ADJUVANT CHEMOTHERAPY WITH UROKINASE (UK) OR UK/WARFARIN FOR RESECTABLE ADENOCARCINOMA OF THE COLON AND RECTUM

Hilgard, P., (London 01-743 2030) Hammersmith Hospital, Dept. of Hematology, Ducane Rd., London W12 OHS England, United Kingdom
PROTOCOL NUMBER(S) UKM-HH-1

OBJECTIVES:

I. Evaluate the efficacy of fibrinolytic therapy with urokinase with or without oral anticoagulation therapy with warfarin as adjuvant treatment for resectable colorectal cancer.

PROTOCOL ENTRY CRITERIA: Patients under 70 years old with Dukes Stage B and C colorectal adenocarcinoma. Patients must be medically eligible for anticoagulant therapy and must not have had long term prior anticoagulant treatment.

PROTOCOL OUTLINE: Randomized study. Patients are randomized following Surgery.

Regimen A: Surgery. Resection of tumor.

Arm I: No therapy.

Arm II: Single-agent Chemotherapy. Urokinase, UK.

Arm III: 2-Drug Combination Chemotherapy. UK; Warfarin, NSC-59813.

STRATIFICATION: Participating institutions; disease stage: A vs. B, C vs. D.

SPECIAL STUDY PARAMETERS: CEA, liver scan, sigmoidoscopy.

END POINTS: Relapse rate, incidence of metastases, survival rate.

CURRENT STATUS: 525 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Surgery. All patients undergo resection of tumor with intraoperative staging. Prophylactic heparin treatment, if given, is recorded and standardized. (Patients with postoperative deep vein thrombosis and/or pulmonary embolism may continue on protocol, but they must be identified and given standardized treatment. Revision, 1980.)

Arm I: No therapy.

Arm II: UK - 250,000 IU iv infusion during ligation, suturing and closure of surgical procedure.

Arm III: UK, as in Arm II; Warfarin - 10 mg po on days 1 and 2. Adjust dose according to clinical parameters (Thrombotest or prothrombin time) and continue Warfarin therapy for 2 years. Follow all patients q 3 months for 2 years and then q 6 months for 3 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/79

2F. GASTROINTESTINAL—GENERAL

2.0121 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED METASTATIC ADENOCARCINOMA OF STOMACH AND PANCREAS

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7931

OBJECTIVES:

I. Determine the antitumor activity of AMSA as determined by response rate and duration of response when used in a single dose schedule in patients with metastatic adenocarcinoma of the stomach and pancreas who have failed on higher priority treatment protocols.

II. Determine the nature and degree of toxicity of this drug.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven, incurable, advanced metastatic adenocarcinoma of stomach or pancreas, who are not eligible for higher priority therapy. Patients must have a minimum life expectancy of 6 weeks, minimum Karnofsky performance status of 50 to 60, and adequate hepatic and hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: Participating institutions; risk status: good vs. poor; prior therapy: Adriamycin (ADR) vs. no ADR.

SPECIAL STUDY PARAMETERS: Liver, bone and brain scans; CEA; hepatic function.

END POINTS: Objective tumor response, response/remission rate, duration of response, toxicity/morbidity of treatment, duration of survival.

CURRENT STATUS: At least 50 patients to be entered.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm (poor-risk patients - over 65 years old, with inadequate marrow reserve or inadequate hepatic or renal function start at 90 mg/sqm) iv on day 1. Repeat course every 21 days or when toxicity permits. Remove patients with unacceptable toxicity or progressive disease after 2 courses. Follow all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 20 and 50 mg ampules.

DATE SUMMARIZED: 02/80

2.0122 PHASE II EVALUATION OF CACP IN PATIENTS WITH RESIDUAL, RECURRENT, OR METASTATIC GASTRIC OR PANCREATIC ADENOCARCINOMA

Woolley, P. V., (202-625-3834) Georgetown University, School of Medicine, 3800 Reservoir Rd., N.W., Washington, District of Columbia, 20007, United States of America

PROTOCOL NUMBER(S) GUMO-11; GIS/GIP8004

OBJECTIVES:

I. Define the activity of cis-platinum in patients with residual, recurrent, or metastatic gastric or pancreatic adenocarcinoma.

PROTOCOL ENTRY CRITERIA: Patients with inoperable, recurrent, residual, or metastatic adenocarcinoma of the stomach or pancreas. Patients must have clearly measurable disease and histologic proof of diagnosis. Patients must have an ECOG performance status of 0-3; adequate hematologic, renal, and hepatic function; and no evidence of active infection.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Drug tolerance.

SPECIAL STUDY PARAMETERS: Tumor measurement, renal function studies, hydrated creatinine clearance, scans and/or x-rays as needed for disease evaluation.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: At least 25 patients will be entered into the protocol.

DOSAGE SCHEDULE:

CACP - 75 mg/sqm iv infusion over 1-2 hours with concomitant mannitol diuresis repeated q 3-4 weeks with escalation to 100 mg/sqm depending on patient tolerance.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/80

2.0123 ADJUVANT CHEMOTHERAPY WITH 5-FU/ADR/MITO FOLLOWING CURATIVE RESECTION FOR ADENOCARCINOMA OF THE STOMACH OR ESOPHAGUS

Karlin, D. A., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-312; MDA-GE-781

OBJECTIVES:

I. Compare disease-free survival and absolute survival in the group treated with 5-fluorouracil (5-FU)/adriamycin (ADR)/mitomycin-C versus historical controls.

PROTOCOL ENTRY CRITERIA: Patients with adenocarcinoma of the stomach or esophagus who have had a curative surgical resection of their primary tumor within the previous 60 days. They must not have had prior chemotherapy, immunotherapy, or radiation for this disease nor have any other concurrent or pre-existent neoplasm.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Length of disease-free interval, survival time.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

5-FU - 600 mg/sqm iv on days 1, 8, 29 and 36; ADR - 30 mg/sqm iv on days 1 and 29; MITO - 10 mg/sqm iv on day 1. Repeat course q 2 months for a total of 1 year.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/79

2.0124 COMBINATION CHEMOTHERAPY WITH MECCNU/5-FU/VCR FOR GASTROINTESTINAL MALIGNANCIES

Stroehlein, J. R., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-376; MDA-M-7901

OBJECTIVES:

I. Determine the efficacy of vincristine (VCR), methyl-CCNU (MeCCNU), and 5-fluorouracil (5-FU), in treatment of gastrointestinal adenocarcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of gastrointestinal adenocarcinoma as measurable disease. Patients must have a life expectancy of at least 12 weeks. The absolute granulocyte count must be more than 2500, platelets more than 150, 000. Direct bilirubin must be less than 2.0 percent, serum creatinine less than 2.5 mg percent.

PROTOCOL OUTLINE: Nonrandomized study. Patients will be entered into one of three regimens on basis of age and previous therapy. Patients 50 years of age or younger with no prior chemotherapy or radiotherapy enter Regimen A; those who are over age 50 with no prior chemotherapy or radiotherapy enter Regimen B. Patients over 50 years of age with prior chemotherapy or radiotherapy enter Regimen C.

Regimen A: 3-Drug Combination Chemotherapy. Methyl-CCNU, MeCCNU, NSC-95441; Vincristine, VCR, NSC-67574; 5-Fluorouracil, 5-FU, NSC-19893.

Regimen B: 3-Drug Combination Chemotherapy. MeCCNU; VCR; 5-FU.

Regimen C: 3-Drug Combination Chemotherapy. MeCCNU; VCR; 5-FU.

STRATIFICATION BY: Age, prior therapy.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Objective tumor response.

CURRENT STATUS: Approximately 50 patients/year are to be given treatment.

DOSAGE SCHEDULE:

Regimen A: VCR - 1 mg/sqm iv on day 1; 5-FU - 375 mg/sqm iv on days 1-5; MeCCNU - 150 mg/sqm po on day 1.

Regimen B: VCR - 1 mg/sqm iv on day 1; 5-FU - 350 mg/sqm iv on days 1-5; MeCCNU - 130 mg/sqm po on day 1.

Regimen C: VCR - 1 mg/sqm iv on day 1; 5-FU - 325 mg/sqm iv on days 1-5; MeCCNU - 120 mg/sqm po on day 1.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

2.0125 IMMUNOTHERAPY WITH BCG IN CANCERS OF THE STOMACH, SMALL BOWEL, BILIARY TRACT, AND PANCREAS

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PROTOCOL NUMBER(S) MI-GI-2

OBJECTIVES:

I. Determine whether immunotherapy with BCG-Tice will improve the remission time and cure rate in patients with cancer of the gastrointestinal tract.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven cancer. The conventional forms of treatment the patient has received will be recorded and he will be treated whether he has undergone potentially curative surgery (adjuvant) or whether he has known residual disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: No further treatment.

STRATIFICATION BY: Participating institutions; staging by the American Joint Committee.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be admitted.

DOSAGE SCHEDULE:

Arm I: BCG - 1 ampule by multiple-puncture tine technique weekly for 3 weeks, divided among both axillae and both groin areas, followed by 12 weekly doses po, adjusted downward if symptoms of gastrointestinal toxicity are seen. After 12-week period, BCG every other week for 2 years.

Arm II: No treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCG - 2-8 x 10 to the eighth colony-forming units/ampule.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

2.0126 SELECTIVE HEPATIC DEARTERIALIZATION, INTRAPERITONEAL BCG AND CHEMOTHERAPY FOR EXTENSIVE INTRA-ABDOMINAL CANCER WITH LIVER METASTASES

Neshat, A. A., Veterans Administration Medical Center, Asheville, North Carolina, 28805, United States of America
PROTOCOL NUMBER(S) NC-GI-1

OBJECTIVES:

I. Determine usefulness of BCG, hepatic dearterialization, and postoperative chemotherapy in treating intra-abdominal cancer with liver metastases.

PROTOCOL ENTRY CRITERIA: Patients with histologic documentation of intra-abdominal cancer with liver metastases (unresectable) due to upper and mid GI, colorectal, biliary or pancreatic cancer

PROTOCOL OUTLINE: Nonrandomized pilot study. Patients are entered following Surgery.

Single-agent Immunotherapy plus Single-agent Chemotherapy. BCG-Glaxo, BCG; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Survival, objective and subjective response.

CURRENT STATUS: 10 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

BCG - 1 ml ampule, ip; 5-FU - iv for 5 days postoperatively.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 00100280

2.0127 PHASE III CHEMOTHERAPY WITH 5-FU VS 5-FU/ADR VS 5-FU/ADR/MITO FOR ADVANCED UPPER GASTROINTESTINAL ADENOCARCINOMA

Dyke, D. R., (507-282-2511) North Central Cancer Treatment Group, 200 1st St. S.W., Rochester, Minnesota, 55091, United States of America
PROTOCOL NUMBER(S) NCCTG-784851

OBJECTIVES:

I. Compare 5-fluorouracil (5-FU) alone vs. 5-FU/adriamycin (ADR) vs. 5-FU/ADR/mitomycin-C (MITO) in the treatment of advanced upper gastrointestinal adenocarcinoma (stomach and pancreas).

PROTOCOL ENTRY CRITERIA: Patients with primary gastric, pancreatic or esophageal columnar mucosal adenocarcinoma. Patients must have measurable, histologically proven, residual, recurrent or metastatic disease not amenable to surgical cure. Patient must have no prior chemotherapy, adequate oral nutrition, and ECOG performance status better than 4. Patients must have adequate bone marrow, hepatic, cardiac and renal function. Enter patients 3 weeks after surgical resection or bypass, 2 weeks after exploration or biopsy or 4 weeks after radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 2-Drug Combination Chemotherapy. 5-FU; Adriamycin, ADR, NSC-123127.

Arm III: 3-Drug Combination Chemotherapy. 5-FU; ADR; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Participating institutions; primary carcinoma: gastric and esophageal mucosal vs. pancreatic; measurable disease; stage of disease: regionally unresectable vs. distant metastasis; ECOG performance status: 0 and 1 vs. 2 and 3.

SPECIAL STUDY PARAMETERS: Hepatic, renal and bone marrow function, liver scan.

END POINTS: Objective tumor response, response/remission rate, duration of response, interval to progression, survival time.

CURRENT STATUS: 300 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: 5-FU - 500 mg/sqm iv on days 1 through 5. Repeat course on day 29 and day 57 and then q 5 weeks or until progression.

Arm II: 5-FU - 400 mg/sqm iv on days 1 through 4; ADR - 50 mg/sqm iv on day 1 (maximum cumulative dose 500 mg/sqm; patients enter Maintenance when this is reached). Repeat course on days 29, 57 and then q 5 weeks or until progression.

Maintenance: 5-FU, as in Arm I.

Arm III: 5-FU - 600 mg/sqm iv on days 1, 8, 29, 36; ADR - 30 mg/sqm iv on days 1 and 29 (maximum cumulative dose 500 mg/sqm. Omit ADR after this dose); MITO - 10 mg/sqm iv on day 1. Repeat course q 8 weeks or until progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/78

2.0128 COMBINATION CHEMOTHERAPY WITH ADR/STZ/MECCNU FOR ADVANCED PANCREATIC, HEPATO-BILIARY AND RELATED CANCER

Douglass, Jr., H. O., (716-633-2796) Roswell Park Memorial Institute, Dept. of Health, 666 Elm Street, Buffalo, New York, 14263, United States of America
PROTOCOL NUMBER(S) RPMI-PPC-523

OBJECTIVES:

I. Establish both the toxicity and response rate of a combination of adriamycin/streptozotocin/methyl-CCNU in patients with advanced pancreatic and hepato-biliary malignancy. (This combination is also being evaluated for pancreatic cancer in a randomized study, EST 2279, by the Eastern Cooperative Oncology Group.)

II. Determine the response rate of this combination in patients with advanced pancreatic and hepato-biliary malignancy initially treated with 5-fluorouracil.

III. Determine the remission duration and survival of patients treated with this 3-drug combination.

IV. Evaluate this combination as Maintenance following radiation–adriamycin combined modality therapy in patients with locally advanced, nonmetastatic, nonresectable cancer.

V. Determine whether there is an effect of vinblastine on human pancreatic neoplasms.

PROTOCOL ENTRY CRITERIA: Patients with nonresectable, histologically proven disease of the following types: hepatocellular carcinoma, cholangiocarcinoma, adenocarcinoma of the gall bladder, bile duct adenocarcinoma, ampullary adenocarcinoma, adenocarcinoma of the pancreas, pancreatic cystadenocarcinoma and related tumors. There must be an evaluable parameter of known malignant disease. Patients must have adequate hematologic, renal and hepatic function. Patients who are not anticoagulated must not have a prothrombin time longer than twice control that is refractory to parenteral vitamin K. Patients must not have severe malnutrition, cachexia, active infection or clinical hepatic encephalopathy. Patients must not receive chemotherapy or radiotherapy to more than 10 percent of bone marrow area within the month preceeding entry. Patients must undergo no surgery involving a bowel or biliary anastomosis within 3 months prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Adriaymcin, ADR, NSC-123127; Streptozotocin, STZ, NSC-85998; Methyl-CCNU, MeCCNU, NSC-95441. At maximum cumulative dose of ADR, 5-Fluorouracil, 5-FU, NSC-19893 is substituted. Patients who fail on this therapy switch to Single-agent Chemotherapy with Vinblastine, VBL, NSC-49842.

STRATIFICATION BY: Measurable vs. evaluable disease, disease category (site of disease, morphology), performance status, prior treatment.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; tumor measurement; CEA; PT; transaminase.

END POINTS: Response/remission rate, duration of remission, survival, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Eighteen patients were entered prior to 1980; based on initial results, further entry has been encouraged.

DOSAGE SCHEDULE:

ADR - 45 mg/sqm rapid iv infusion on day 1 q 3 weeks to a total cumulative dose of 550 mg/sqm; MeCCNU - 60 mg/sqm po on day 1 q 3 weeks; STZ - 400 mg/sqm rapid iv infusion on days 1 through 5 q 6 weeks. Patients who are ineligible for ADR and those who continue therapy after receiving the total cumulative dose of ADR receive 5-FU - 400 mg/sqm iv on days 1 through 5 during STZ courses and 600 mg/sqm on day 1 of intervening courses. Patients will stop ADR/STZ/MeCCNU therapy upon documentation of progression and will be treated with VBL - 0.2 mg/kg/week iv until further progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 20 mg vials; STZ - 2 gm vials; MeCCNU - 10, 20, 50 and 100 mg capsules.

DATE SUMMARIZED: 10/80

2.0129 RADIOTHERAPY AND CHEMOTHERAPY WITH ADR FOR LOCALIZED, UNRESECTABLE CARCINOMA OF THE STOMACH, PANCREAS, AND BILIARY TREE

Douglas, H. O., (716-845-3306) Roswell Park Memorial Inst., 666 Elm St., Buffalo, New York, 14263, United States of America
PROTOCOL NUMBER(S) RPMI-PPC-524

OBJECTIVES:

I. Evaluate the base tolerance and tumor response to radiotherapy complemented by adriamycin given at a dose level that does not potentiate the systemic effects of radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients with localized, unresectable carcinoma of the stomach, pancreas, biliary tract, regional lymph nodes, and regional peritoneum. Area of malignant disease must not exceed 400 sq cm.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy plus Single-agent Chemotherapy. Supervoltage radiation plus Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Not applicable.

SPECIAL STUDY PARAMETERS: Performance status (ECOG scale), IVP, liver scans.

END POINTS: Time to regional recurrence, time to development of metastases, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Approximately 25 patients will be entered, no more than 10 in any disease category.

DOSAGE SCHEDULE:

Beginning on day 1 give 4000 rads to upper abdomen (treatment field must not exceed 400 sq cm) over 4.5 weeks; plus ADR - 15 mg/sqm iv initial dose on day 5, then 10 mg/sqm iv once a week given within one hour of completion of Radiotherapy for the duration of Radiotherapy. Total ADR dose must not exceed 550 mg/sqm. Withhold therapy for 2 weeks following laparotomy and for 3 weeks following intestinal resection or bypass.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: ADR - 50 mg vials.

DATE SUMMARIZED: 10/76

2.0130 PHASE II ADJUVANT COMBINATION CHEMOTHERAPY WITH 5-FU/MECCNU PLUS BCG IMMUNOTHERAPY IN GASTROINTESTINAL CANCER

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PROTOCOL NUMBER(S) CAN-CCI-GI-1

OBJECTIVES:

I. Determine the efficacy of 2-drug combination chemotherapy with 5-fluorouracil and methyl-CCNU plus immunotherapy with BCG vs. BCG alone vs. no treatment in terms of survival for patients with resectable cancer of stomach, colon and rectum.

PROTOCOL ENTRY CRITERIA: Patients with gastric, colonic or rectal adenocarcinoma, after curative resection; Stages T(1-4), N(1-2), M(0); Dukes Stages B2 or C.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy plus Immunotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Methyl CCNU, MeCCNU, NSC-95441; BCG Connaught, BCG, NSC-B116341.

Arm II: Immunotherapy. BCG.

Arm III: No further adjuvant post-operative treatment.

STRATIFICATION BY: Colon and rectum by Dukes Stages B2 and C.

SPECIAL STUDY PARAMETERS: CEA.

END POINTS: Recurrence/survival rate, length of survival, toxicity, morbidity.

CURRENT STATUS: 150 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: 5-FU - 375 mg/sqm iv on days 1-5; MeCCNU - 120 mg po on day 1; 5-FU - 325 mg/sqm iv on days 36-40; plus BCG - 120 mg po on days 28 and 63. Repeat q 10 weeks for 8 courses maximum, followed by BCG as in Arm II for 5 years.

Arm II: BCG - 120 mg po q 28 days for 5 years.

Arm III: No further adjuvant post-operative treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCG - 40 mg, lyophilized; MeCCNU - 20, 50, and 100 mg capsules.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 01500280

2.0131 POST-SURGICAL ADJUVANT BCG IMMUNOTHERAPY AND 5-FU CHEMOTHERAPY FOR ADENOCARCINOMA OF THE STOMACH, PANCREAS, COLON OR RECTUM

Falk, R. E., (416-595-4148) Toronto General Hospital, 101 College Street, Toronto, Ontario, M5G 1L7, Canada
PROTOCOL NUMBER(S) CAN-UICC-7501; CAN-TGH-7501

OBJECTIVES:

I. Evaluate the effect of immunostimulation with BCG given as a single dose intraperitoneally followed by oral administration combined with chemotherapy with 5-FU vs. chemotherapy with 5-FU alone in the following high-risk circumstances: 1. In gastric and pancreatic adenocarcinomas resected for cure - to determine if the recurrence-free period and survival are prolonged; 2. In adenocarcinoma of the stomach, pancreas, colon and rectum where only palliative surgery is possible -to determine if tumor regression can be achieved and survival time prolonged.

PROTOCOL ENTRY CRITERIA: Adenocarcinoma of the gastrointestinal tract: patients with carcinoma of the colon or rectum who have undergone palliative surgery and patients with carcinoma of the pancreas or stomach who have had either palliative or curative surgery. Patients must be in clinical condition adequate to tolerate treatment, and must not have received prior chemotherapy, radiotherapy or immunotherapy with BCG or C. parvum.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery and Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: Surgery, Single-agent Chemotherapy and Immunotherapy. 5-FU, BCG - type not stated.

STRATIFICATION BY: Tumor site: stomach vs. pancreas vs. colon; participating institutions.

SPECIAL STUDY PARAMETERS: Endoscopy, angiography, radioisotope studies to determine extent of disease, immunologic skin tests, performance status.

END POINTS: Length of survival, disease-free interval, objective tumor responses, response/remission rate, quality of survival.

CURRENT STATUS: 200 patients were to be entered in about 2 years.

DOSAGE SCHEDULE:

Arm I: Begin 3 weeks following surgery. Loading dose: 5-FU - 15 mg/kg iv on days 1-4, then 5-FU - 'Standard dose' (amount not given) iv q 7 days for 3 weeks. Repeat course q 4 weeks until death of patient.

Arm II: At time of surgery: BCG - 2 mg ip or by dialysis catheter within 1 month of resection. 3 weeks later give 5-FU - loading dose as in Arm I, followed one week later by BCG - 120 mg po. Repeat BCG - po q 4 weeks. One week following 1st BCG-po dose begin 5-FU - 'standard dose' - as in Arm I. Continue therapy until death of patient.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/78

2.0132 DOUBLE-BLIND EVALUATION OF ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE PRE- AND POST-OPERATIVELY FOR GASTROINTESTINAL CANCER

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PROTOCOL NUMBER(S) ITA-GI-1; ITA-GFGT-50/80

OBJECTIVES:

I. Evaluate in a double blind trial the efficacy of adjuvant immunotherapy using levamisole preoperatively and postoperatively in patients undergoing resective surgery for cancer of the esophagus, stomach, or colon.

II. Determine the effect of total parenteral nutrition on the immune status.

PROTOCOL ENTRY CRITERIA: Patients with cancer of the esophagus, stomach, or colon, with or without metastases.

PROTOCOL OUTLINE: Study randomized (double-blind) for Immunotherapy. All patients are treated by Surgery or by Surgery plus total parenteral nutrition. Malnourished patients receive triphosphopyridine nucleotide and nutritional monitoring.

Arm I: Single-agent Immunotherapy. Levamisole, LEV, NSC-177023.

Arm II: Placebo.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Immunological monitoring, CEA.

END POINTS: Analysis of immunological multitest monitoring in the followup of treated patients; survival.

CURRENT STATUS: 30 patients have been entered.

DOSAGE SCHEDULE:

Arm I: LEV - 2.5 mg/kg po 3 days preoperatively and twice weekly postoperatively as soon as oral intake is possible.

Arm II: Placebo.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: LEV - 50 mg tablets.

DATE SUMMARIZED: 01/81

2.0133 IMMUNOCHEMOTHERAPY WITH LEVAMISOLE, MITO, AND FT-207 VS CHEMOTHERAPY WITH MITO AND FT-207 FOR GASTROINTESTINAL CANCER

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PROTOCOL NUMBER(S) JAP-GI-1

OBJECTIVES:

I. Compare survival improvement in gastric and colorectal cancer treated with immunochemotherapy with levamisole, mitomycin-C, and ftorafur vs. chemotherapy with MITO and FT-207.

PROTOCOL ENTRY CRITERIA: Patients with gastric and colorectal cancer.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. Mitomycin-C, MITO, NSC-26980; Ftorafur, FT-207, NSC-148958.

Arm II: 2-Drug Combination Chemotherapy plus Immunotherapy. MITO; FT-207; plus Levamisole, LEV, NSC-177023.

STRATIFICATION BY: Prior surgery vs. no prior surgery.

SPECIAL STUDY PARAMETERS: Mitogen response of lymphocytes, skin tests (PPD, PHA), peripheral lymphocyte counts, and several cytotoxic T-cell functions.

END POINTS: Recurrence/survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 500 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: MITO - 0.08 mg/kg iv twice a week for 10 times; FT-207 - 600-800 mg/day po for two years, started 7 days after surgery.

Arm II: Arm I plus LEV - 150 mg/day po three consecutive days every other week for two years, started three days before surgery.

Dosage modifications for toxicity are given.

DOSAGE FORMS: LEV - 50 mg tablets.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 05000280

2.0134 IMMUNOTHERAPY WITH BCG, PSK, OK-432 WITH/WITHOUT CHEMOTHERAPY WITH FT ADJUVANT TO SURGERY FOR ADVANCED GASTROINTESTINAL CANCER

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PROTOCOL NUMBER(S) JAP-GI-2

OBJECTIVES:

I. Determine the value of living BCG in patients with advanced gastrointestinal cancer, Stages III and IV.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven cancer of the gastrointestinal tract involving regional lymph nodes (Stage III) or adjacent organs and distant lymph nodes (Stage IV).

PROTOCOL OUTLINE: Double-blind randomized study. Patients are randomized following surgery.

Arm I: Single-agent Immunotherapy. BCG-unspecified, BCG.

Arm II: 2-Agent Immunotherapy. BCG; PSK.

Arm III: 2-Agent Immunotherapy plus Single-agent Chemotherapy. BCG; PSK; Ftorafur, FT-207, NSC-148958.

Arm IV: Single-agent Immunotherapy. PSK.

Arm V: Single-agent Immunotherapy. Picibanil, OK-432, NSC-293562.

Arm VI: 2-Agent Immunotherapy. BCG; OK-432.

Arm VII: No further treatment.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Skin tests: DNCB, PPD, KLH, PHA-P; T and B cell enumeration; lymphocyte response to PHA; random mobility of leukocytes; macrophage chemotactic activity.

END POINTS: Duration of response, survival rate.

CURRENT STATUS: 1200 patients have been entered as of July 1980.

DOSAGE SCHEDULE:

Arm I: BCG - 1 x 10 to the ninth viable organisms id within 5-10 days of surgery.

Arm II: BCG as in Arm I; PSK (dosage and schedule not given).

Arm III: BCG as in Arm I; PSK; FT-207 (dosage and schedule not given).

Arm IV: PSK (dosage and schedule not given).

Arm V: OK-432 (dosage and schedule not given).

Arm VI: BCG as in Arm I; OK-432 (dosage and schedule not given).

Arm VII: No further therapy.

All patients receive additional BCG at regular intervals for maintenance of their immunocompetence.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 10/80

SECTION 3

GENITOURINARY TUMORS

3A. BLADDER

NBCCGA-7 ADJUVANT CHEMOTHERAPY WITH CIS-PLATINUM FOR INVASIVE CARCINOMA OF THE BLADDER 3.0001
NCOG-4B81 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM/ADRIAMYCIN/CYCLOPHOSPHAMIDE VS CIS-PLATINUM FOR METASTATIC TRANSITIONAL CELL BLADDER CANCER 3.0002
NCOG-4B82 PHASE III MNI OR CACP WITH PREOPERATIVE RADIOTHERAPY FOR LOCAL CONTROL OF BLADDER CANCER AND CACP FOR DISTANT METASTASES 3.0003
RTOG-7705 RADIOTHERAPY WITH NEUTRONS ALONE OR WITH PHOTONS WITH OR WITHOUT SURGERY FOR URINARY BLADDER CANCER 3.0004
RTOG-7804 ADJUVANT RADIOTHERAPY BEFORE AND AFTER SURGERY FOR BLADDER CANCER 3.0005
RTOG-7826 PHOTON RADIOTHERAPY VS PION RADIOTHERAPY FOR TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER 3.0006
SEG-78BL0103 PHASE III ADJUVANT CHEMOTHERAPY WITH CTX/ADR/CACP FOR RESECTED TRANSITIONAL CELL BLADDER CARCINOMA 3.0007
SEG-79BL351 PHASE III CHEMOTHERAPY WITH CTX/ADR/CACP VS CACP FOLLOWED BY MAINTENANCE OR NO THERAPY FOR METASTATIC BLADDER CARCINOMA 3.0008
SWOG-7904 PHASE II-III HMM VS FAC (5-FU/ADR/CTX) CHEMOTHERAPY FOR ADVANCED TRANSITIONAL CELL BLADDER CANCER WITH IMPAIRED RENAL FUNCTION 3.0009
SWOG-7922 PHASE II-III CHEMOTHERAPY WITH CAP-I (CTX/ADR/CACP) VS AMSA FOR ADVANCED TRANSITIONAL CELL CANCER OF THE URINARY BLADDER 3.0010
UORG-06 CHEMOTHERAPY WITH HMM FOR METASTATIC TRANSITIONAL-CELL CARCINOMA OF THE BLADDER 3.0011
MDAR-163 CHEMOTHERAPY WITH INTRAVESICAL MITOMYCIN-C FOR SUPERFICIAL URINARY BLADDER TUMORS (STAGES O/A) 3.0012
MDAR-219 ADJUVANT CHEMOTHERAPY WITH ADRIAMYCIN FOLLOWING RADIOTHERAPY AND CYSTECTOMY FOR INFILTRATING CARCINOMA OF THE BLADDER 3.0013
MDAR-347 INTRAVESICAL CHEMOTHERAPY WITH THIOTEPA VS MITOMYCIN-C FOR NON-INVASIVE TRANSITIONAL BLADDER CARCINOMA 3.0014
MSKCC-7766 BCG PLUS FULGURATION VS FULGURATION ALONE FOR RECURRENT MULTICENTRIC SUPERFICIAL BLADDER CANCER 3.0015
MI-BL-1 ADJUVANT IMMUNOTHERAPY WITH BCG FOR BLADDER CANCER 3.0016
TX-UTHSC-BL-1 IMMUNOTHERAPY WITH INTRAVESICULAR AND PERCUTANEOUS BCG ADJUVANT TO SURGERY IN RECURRENT SUPERFICIAL BLADDER CANCER 3.0017
BRA-LACRIP-031 INTRAVESICULAR ADR FOLLOWING TRANSURETHRAL RESECTION FOR NON-METASTATIC BLADDER WALL PAPILLARY CARCINOMA 3.0018

EORTC-30781 PHASE III VITAMIN THERAPY WITH PYRIDOXINE FOR RESECTED TRANSITIONAL CELL TUMORS OF THE BLADDER 3.0019
EORTC-30782 PHASE III CHEMOTHERAPY WITH THIOTEPA OR CACP OR ADR FOR RECURRENT RESECTABLE TA OR T1 PAPILLARY CARCINOMA OF THE BLADDER 3.0020
EORTC-30784 PHASE III CHEMOTHERAPY WITH ADR/5-FU FOLLOWING RADICAL CYSTECTOMY WITH OR WITHOUT RADIOTHERAPY FOR CARCINOMA OF THE BLADDER 3.0021
EORTC-30790 PHASE III CHEMOTHERAPY WITH ADR OR EPODYL FOR RESECTED T1 AND TA PAPILLARY CARCINOMA OF THE BLADDER 3.0022
EORTC-30797 PHASE II CHEMOTHERAPY WITH VINCRISTINE FOR ADVANCED CARCINOMA OF THE BLADDER 3.0023
UICC-78025 ADJUVANT CHEMOTHERAPY WITH ADRIAMYCIN/5-FLUOROURACIL FOLLOWING RADICAL RADIOTHERAPY FOR T3, NX, M0 BLADDER CARCINOMA 3.0024
UKM-BL-1 IMMUNOTHERAPY WITH TUMOR-IMMUNE PIG LYMPH NODE CELLS PLUS RADIOTHERAPY VS RADIOTHERAPY ALONE FOR URINARY BLADDER CANCER 3.0025
URU-BL-1 SINGLE-AGENT CHEMOTHERAPY WITH VM-26 VS CHEMO/IMMUNOTHERAPY WITH VM-26, LEVAMISOL IN RESIDUAL DETECTABLE URINARY BLADDER CANCER 3.0026
URU-BL-2 COMPARISON OF ADJUVANT CHEMOTHERAPY WITH VM-26 AND ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE FOR NONDETECTABLE CARCINOMA OF THE BLADDER 3.0027

3B. KIDNEY

SEG-GU-P33 PHASE II CHEMOTHERAPY WITH VBL/CCNU/HU AND HORMONE THERAPY WITH MEDROXYPROGESTERONE ACETATE FOR METASTATIC RENAL ADENOCARCINOMA 3.0028
SWOG-7956 PHASE II POSTINFARCTION NEPHRECTOMY PLUS MEDROXYPROGESTERONE ACETATE FOR METASTATIC RENAL CELL CARCINOMA 3.0029
SWOG-7959 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR METASTATIC RENAL CELL CARCINOMA 3.0030
SWOG-8011 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE (DHAD) FOR ADVANCED RENAL CELL CARCINOMA 3.0031
BCRP-7817 TAMOXIFEN AND MEDROXYPROGESTERONE ACETATE FOR DISSEMINATED RENAL CELL CARCINOMA 3.0032
BCRP-7921 PHASE II EVALUATION OF METHYL-GAG IN PATIENTS WITH DISSEMINATED CARCINOMA OF THE KIDNEY 3.0033
BCRP-8031 PHASE II CHEMOTHERAPY WITH CL 216,942 ON A SINGLE-DOSE SCHEDULE FOR ADVANCED RENAL CELL CARCINOMA 3.0034
MDAR-162 PERCUTANEOUS TRANSFEMORAL RENAL ARTERY OCCLUSION, NEPHRECTOMY AND HORMONAL THERAPY WITH MEDROXYPROGESTERONE ACETATE FOR RENAL CARCINOMA 3.0035
MDAR-316 ORAL ESTRACYT FOR METASTATIC RENAL CARCINOMA 3.0036
MDAR-327 PHASE II-III CHEMOTHERAPY WITH CONTINUOUS 5-DAY VINDESINE INFUSION FOR METASTATIC RENAL CARCINOMA 3.0037
MSKCC-796 IMMUNOTHERAPY WITH BCG AND RENAL CANCER CELLS FOR STAGE II-IV RENAL CANCER 3.0038
OH-REN-OSU-7902 CROSS-OVER IMMUNOTHERAPY WITH POLYMERIZED TUMOR ANTIGEN-ADJUVANT AND HORMONAL THERAPY WITH PROGESTERONE FOR RENAL CANCER 3.0039
PA-MSHMC-REN-1 ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE FOR STAGE II AND III RENAL CELL CARCINOMA 3.0040
EORTC-30801 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED RENAL CELL CARCINOMA 3.0041

3C. PROSTATE

EST-PB-879 PILOT IMMUNOTHERAPY WITH LEVAMISOLE ADJUVANT TO DIETHYLSTILBESTROL THERAPY FOR STAGE D ADENOCARCINOMA OF THE PROSTATE 3.0042
EST-PD-879 PHASE II PILOT CHEMOTHERAPY WITH CACP FOR ADVANCED (STAGE D) PROSTATIC CARCINOMA 3.0043
NCOG-4P81 PHASE III ADR VS ADR/CIS-PLATINUM CHEMOTHERAPY FOR ENDOCRINE UNRESPONSIVE METASTATIC ADENOCARCINOMA OF THE PROSTATE 3.0044
NCOG-4P82 PHASE III THERAPY WITH DES VS DES/ADR FOR METASTATIC ADENOCARCINOMA OF THE PROSTATE 3.0045
NPCP-1000 RADIOTHERAPY FOLLOWED BY ESTRACYT OR CTX FOR PROSTATIC ADENOCARCINOMA 3.0046
NPCP-1100 COMPARISON OF ESTRACYT, CACP, AND MTX AS SINGLE AGENTS IN HORMONE-REFRACTORY PATIENTS WITH ADVANCED PROSTATIC CANCER 3.0047
NPCP-1200 COMPARISON OF CACP VS ESTRACYT VS CACP/ESTRACYT IN STAGE D PROSTATIC CARCINOMA FOLLOWING EXTENSIVE RADIOTHERAPY 3.0048
NPCP-1300 DES OR ORCHIECTOMY VS CTX/5-FU PLUS DES OR ORCHIECTOMY VS ESTRACYT FOR STAGE D PROSTATE CANCER WITHOUT PRIOR HORMONAL THERAPY OR CHEMOTHERAPY 3.0049
NPCP-600 HORMONE THERAPY WITH DES ALONE OR COMBINED WITH CTX OR ESTRACYT FOR PROSTATIC CARCINOMA STAGE D 3.0050
NPCP-900 HORMONE THERAPY WITH ESTRACYT VS CHEMOTHERAPY WITH CTX AFTER PROSTATECTOMY FOR PROSTATIC ADENOCARCINOMA 3.0051
RTOG-7506 RADIOTHERAPY AND HORMONAL THERAPY WITH STILPHOSTROL FOR STAGE C ADENOCARCINOMA OF THE PROSTATE 3.0052
RTOG-7704 RADIOTHERAPY USING NEUTRONS ALONE OR IN COMBINATION WITH PHOTONS FOR STAGE C ADENOCARCINOMA OF THE PROSTATE 3.0053
RTOG-7706 PROSTATIC IRRADIATION VS PELVIC IRRADIATION PLUS PROSTATE BOOST FOR STAGE A2 AND B PROSTATIC ADENOCARCINOMA 3.0054
SEG-78PR0103 SEQUENTIAL VS CONCURRENT CHEMOTHERAPY WITH DIETHYLSTILBESTROL AND CYCLOPHOSPHAMIDE FOR STAGE IV PROSTATIC CARCINOMA 3.0055
SWOG-8010 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE (DHAD) FOR ADVANCED PROSTATE CANCER 3.0056
MAYO-795201 PHASE II HORMONE THERAPY WITH TAMOXIFEN FOR ADVANCED ADENOCARCINOMA OF THE PROSTATE 3.0057
MAYO-795202 PHASE II COMBINATION CHEMOTHERAPY WITH CAP (CTX/ADR/CDDP) AND CTX/CDDP FOR ADVANCED ADENOCARCINOMA OF THE PROSTATE 3.0058
MDAR-325 HORMONE THERAPY WITH TAMOXIFEN FOR METASTATIC ADENOCARCINOMA OF THE PROSTATE 3.0059
MDAR-407 COMBINATION CHEMOTHERAPY WITH FAM (5-FU/ADR/MITO-C) ALTERNATING WITH FA (5-FU/ADR) FOR ADVANCED PROSTATIC CARCINOMA 3.0060
NCI-78-C-56 CHEMOTHERAPY WITH ADR/CTX/CACP FOLLOWED BY ORCHIECTOMY FOR CHEMOTHERAPY FAILURES IN PATIENTS WITH METASTATIC PROSTATIC CARCINOMA 3.0061
WSU-C-31279 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED METASTATIC PROSTATIC CARCINOMA 3.0062
IL-PR-1 ADJUVANT IMMUNOTHERAPY WITH BCG FOR PROSTATIC CARCINOMA 3.0063
CAN-NCIC-PR1 RADIOTHERAPY VS HORMONE THERAPY WITH DES OR ORCHIECTOMY FOR STAGE C AND D1 CARCINOMA OF THE PROSTATE 3.0064
EORTC-30761 COMPARATIVE STUDY OF HORMONE THERAPY WITH CTA, MPA, OR DES FOR ADVANCED PROSTATIC CANCER STAGE T3 AND T4 ...... 3.0065
EORTC-30762 COMPARISON OF SINGLE-AGENT HORMONE THERAPY WITH ESTRACYT VS DIETHYLSTILBESTROL FOR ADVANCED PROSTATIC CANCER, STAGE T3 AND T4 ...... 3.0066

EORTC-30799 PHASE II CHEMOTHERAPY WITH VINDESINE FOR REFRACTORY ADVANCED PROSTATIC CARCINOMA 3.0067

3D. TESTIS

NCOG-4T81 PHASE III STUDY OF RETROPERITONEAL NODE SURGERY VS IRRADIATION FOR STAGE I NONSEMINOMATOUS TUMORS OF THE TESTIS 3.0068
NCOG-4T82 COMBINATION CHEMOTHERAPY WITH CACP/VBL/BLEO WITH & WITHOUT LITHIUM CARBONATE NEUTROPENIA ATTENUATION FOR GERMINAL CELL TUMORS IN MALES 3.0069
SEG-GU-P47 PHASE II REINDUCTION CHEMOTHERAPY WITH VP-16/CACP/ADR/BLEO FOLLOWING PROGRESSION ON VBL MAINTENANCE FOR TESTICULAR CANCER 3.0070
SEG-78GU0102 PHASE II CACP/VBL/BLEO WITH OR WITHOUT ADR INDUCTION CHEMOTHERAPY PLUS VBL MAINTENANCE FOR DISSEMINATED TESTICULAR CARCINOMA 3.0071
SWOG-7817 PHASE III LOW VS HIGH DOSE CACP PLUS VBL/BLEO FOLLOWED BY SURGERY & CTX/ACT-D/ADR/VBL MAINTENANCE FOR TESTICULAR GERM CELL NEOPLASMS 3.0072
TCIS-TC-179/179R SURGERY WITH OR WITHOUT VAB-V (VBL/ACT-D/CTX/BLEO/CACP) FOR STAGE II NON-SEMINOMATOUS, NON-CHORIOCARCINOMA TESTICULAR GERM CELL TUMORS 3.0073
TCIS-TC-279/279R SURGERY WITH OR WITHOUT VBP CHEMOTHERAPY FOR STAGE II NON-SEMINOMATOUS, NON-CHORIOCARCINOMA TESTICULAR GERM CELL TUMORS 3.0074
MDAR-148 CHEMOTHERAPY WITH VBL/BLEO AND INTRAVENOUS HYPERALIMENTATION FOR TESTICULAR CANCER 3.0075
MDAR-175 COMBINATION CHEMOTHERAPY WITH VBL/BLEO AND SEQUENTIAL CHEMOTHERAPY WITH CACP FOR ADVANCED TESTICULAR AND EXTRAGONADAL CANCER 3.0076
MDAR-370 HIGH-DOSE COMBINATION CHEMOTHERAPY WITH CTX/VP-16 PLUS IMMUNOTHERAPY WITH BMT AND MAINTENANCE WITH ADR/VP-16 FOR TESTICULAR CARCINOMA 3.0077
MSKCC-7939 CHEMOTHERAPY WITH CTX/VBL/ACT-D/BLEO/CACP PLUS SURGERY FOR DISSEMINATED NONSEMINOMATOUS GERM CELL TUMORS 3.0078
NCI-77-C-25 REDUCTIVE SURGERY PLUS CHEMOTHERAPY (CTX/VBL/ACT-D/BLEO/CACP) VS CHEMOTHERAPY ALONE FOR NONSEMINOMATOUS TESTICULAR TUMORS 3.0079
ARG-CMH-7806 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM/BLEOMYCIN/VINBLASTINE/VP-16 FOR ADVANCED NONSEMINOMATOUS TESTICULAR CARCINOMA 3.0080
DAN-DATECA-6 CHEMOTHERAPY WITH BLEO/VBL/ACT-D WITH OR WITHOUT CIS-PLATINUM FOR STAGE III NON-SEMINOMATOUS CARCINOMA OF THE TESTIS 3.0081
EORTC-30795 PHASE III INDUCTION CHEMOTHERAPY WITH CACP, VBL, BLEO FOR DISSEMINATED TESTICULAR NON-SEMINOMA 3.0082
EORTC-30796 MAINTENANCE CHEMOTHERAPY WITH CACP/VBL FOR TESTICULAR NON-SEMINOMA IN COMPLETE REMISSION 3.0083

3E. GENITOURINARY—GENERAL

EST-1878 PHASE III STUDY WITH CACP VS ADR/CTX/CACP & PHASE II STUDY WITH VM-26 FOR DISSEMINATED TRANSITIONAL CELL URINARY TRACT CANCER 3.0084
EST-1879 CHEMOTHERAPY WITH MITOTANE PLUS HORMONE REPLACEMENT FOR ADRENAL CORTICAL CARCINOMA AND CHEMOTHERAPY WITH ADR FOR TUMORS UNRESPONSIVE TO MITOTANE 3.0085
NBCP-6A PHASE II CIS-PLATINUM CHEMOTHERAPY WITH OR WITHOUT CTX/ADR FOR ADVANCED TRANSITIONAL CELL CANCER OF THE BLADDER, URETER, OR RENAL PELVIS 3.0086
NBCP-6B PHASE II HEXAMETHYLMELAMINE VS CIS-PLATINUM THERAPY FOR ADVANCED TRANSITIONAL CELL CANCER OF THE BLADDER, URETER, OR RENAL PELVIS 3.0087

NBCP-6C PHASE II VP-16 VS CIS-PLATINUM CHEMOTHERAPY FOR ADVANCED TRANSITIONAL CELL CANCER OF THE BLADDER, URETER, OR RENAL PELVIS 3.0088

SEG-GU-P45 PHASE II CHEMOTHERAPY WITH VP-16213 FOR INCURABLE OR METASTATIC CARCINOMA OF THE BLADDER AND PROSTATE 3.0089

SWOG-7916 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE FOR METASTATIC MALIGNANCIES OF THE TESTES, BLADDER, PROSTATE AND KIDNEY 3.0090

SWOG-7937 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED METASTATIC CARCINOMA OF THE GENITOURINARY TRACT 3.0091

MAYO-805101 PHASE II COMBINATION CHEMOTHERAPY WITH VP-16/CACP FOR ADVANCED TRANSITIONAL CELL CANCER OF THE BLADDER, URETER, AND RENAL PELVIS 3.0092

MAYO-805501 PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE (AZQ) FOR ADVANCED GENITOURINARY CARCINOMA 3.0093

MDAR-289 CHEMOTHERAPY WITH CACP VS CTX/ADR/CACP FOR METASTATIC TRANSITIONAL CELL CARCINOMA OF THE URINARY TRACT 3.0094

MSKCC-7818 CHEMOTHERAPY WITH CIS-PLATINUM/CYCLOPHOSPHAMIDE/ADRIAMYCIN FOR NONRESECTABLE ADVANCED METASTATIC UROTHELIAL TUMORS 3.0095

DUT-AZL-1 MITOTANE AND/OR PHASE II CHEMOTHERAPY WITH CAP-I (CTX/ADR/CACP) FOR MAXIMALLY RESECTED ADRENOCORTICAL CARCINOMA 3.0096

SECTION 3

GENITOURINARY TUMORS

3A. BLADDER

3.0001 ADJUVANT CHEMOTHERAPY WITH CIS-PLATINUM FOR INVASIVE CARCINOMA OF THE BLADDER

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PROTOCOL NUMBER(S) NBCCGA-7

OBJECTIVES:

I. Test in a controlled, randomized trial the hypothesis that cis-platinum administered to patients with bladder carcinoma following preoperative radiation and radical cystectomy will increase the 5-year survival rate by at least 20%.

PROTOCOL ENTRY CRITERIA: Patients with primary carcinoma of the bladder with microscopic evidence of muscle invasion, and residual tumor following cystectomy and pelvic lymph node dissection but no metastases to distant sites, contiguous organs or lymph nodes at or above the biforcation of the common iliac arteries. Patients must not be over 75 years old with adequate bone marrow function and a performance status of 0, 1 or 2. Patients must be eligible for radiotherapy and radical cystectomy prior to adjuvant chemotherapy.

PROTOCOL OUTLINE: Randomized study. Following treatment on Regimen A, patients are randomized to Arms I and II.

Regimen A: Surgery plus Radiotherapy. Transurethral resection (TUR) followed by low-LET, megavoltage, external beam irradiation followed by radical cystectomy.

Arm I: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: No further therapy.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Cystoscopy, excretory urogram, bone and liver scans, audiogram.

END POINTS: Survival rate, survival time, disease free interval, toxicity/morbidity of treatment, site and nature of recurrence.

CURRENT STATUS: 180 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Regimen A: Transurethral resection; 0 to 3 weeks following TUR, 4000 rads to pelvic tumor in 4.5 weeks; followed within 1 to 4 weeks by radical cystectomy.

Arm I: CACP - 70 mg/sqm iv on day 1 with adequate hydration. Repeat course q 3 weeks for a total of 8 courses.

Arm II: No further therapy.

Follow all patients for at least 5 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 00040379

3.0002 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM/ADRIAMYCIN/CYCLOPHOSPHAMIDE VS CIS-PLATINUM FOR METASTATIC TRANSITIONAL CELL BLADDER CANCER

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PROTOCOL NUMBER(S) NCOG-4B81

OBJECTIVES:

I. Compare combination chemotherapy with cis-platinum/adriamycin/cyclophosphamide to single-agent chemotherapy with cis-platinum for metastatic transitional cell carcinoma of the urinary bladder.

II. Define differences of response rates based on degree of histologic differentiation, initial performance status and prior radiation or systemic chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients up to 75 years of age with measurable, histologically-proven and graded transitional cell carcinoma of the urinary bladder with clinically-demonstrated metastatic disease. Patients must have life expectancy of at least 6 weeks, performance status of at least 60, and adequate renal and bone marrow function. Patients must not have had chemotherapy, extensive radiotherapy or major surgery within the 3 weeks prior to entry.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm II: Single-agent Chemotherapy. CACP.

STRATIFICATION BY: Participating institutions; Karnofsky performance status: 80-100 vs. 60-70; prior radiotherapy, prior cystectomy; histology: well differentiated vs. moderately well differentiated vs. undifferentiated.

SPECIAL STUDY PARAMETERS: Bone and liver scan, bone marrow biopsy, lung tomographs, CAT scan, Echo.

END POINTS: Objective tumor response, response/remission rate, duration of response, time to response, survival time.

CURRENT STATUS: 100 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: CTX - 650 mg/sqm iv given over 15 minutes; ADR - 50 mg/sqm (maximum cumulative dose 450 mg/sqm) iv immediately after CTX; CACP - 100 mg/sqm iv with intravenous hydration and diuresis in 6 divided doses over 24 hours immediately after ADR.

Arm II: CACP - as in Arm I.

Repeat courses in both Arms q 3 weeks for at least 2 courses. Continue therapy for 2 years or until patient has progressive disease. Follow patients until time of recurrence and death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; ADR - 10 mg ampules; CTX - 100 and 500 mg ampules.

DATE SUMMARIZED: 11/78

3.0003 PHASE III MNI OR CACP WITH PREOPERATIVE RADIOTHERAPY FOR LOCAL CONTROL OF BLADDER CANCER AND CACP FOR DISTANT METASTASES

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PROTOCOL NUMBER(S) NCOG-4B82

OBJECTIVES:

I. Evaluate the pathological downstaging seen at 21-28 days following 2000 rads of radiotherapy in 1 week to the bladder, and compare this with the same irradiation plus cis-platinum and the same irradiation plus misonidazole in patients with transitional cell carcinoma of the bladder of Stages T2-T4, P1-P4.

II. Evaluate the effect of each treatment on the incidence of positive nodes found at surgery.

III. Study time to progression and patterns of recurrence in each preoperative group.

IV. Study the effect of cis-platinum adjuvant chemotherapy on relapse patterns, time to progression, and survival for high-risk patients following cystectomy.

PROTOCOL ENTRY CRITERIA: Patients with biopsy or cytology proven transitional cell carcinoma of Stages T2-T4 (AJC or UICC) and B1-D1 (Jewett) who do not have distant metastases and who have a Karnofsky performance status of at least 60 percent. Patients may not be over 75 years of age and must have adequate bone marrow, hepatic, and renal function. Patients must not have had prior irradiation of the pelvic region, prior systemic chemotherapy, or another malignant neoplasm except skin cancer within the 5 years prior to entry.

PROTOCOL OUTLINE: Randomized study.

Regimen A: Preoperative Treatment. Randomize to Arms I, II, or III.

Arm I: Radiotherapy. Megavoltage treatment of the pelvic region with peak photon energies of at least 4 MeV.

Arm II: Radiotherapy plus Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm III: Radiotherapy plus Hypoxic Cell Sensitization. Misonidazole, MNI, NSC-261037. (This arm to be activated when MNI becomes available.)

Regimen B: Resective Surgery.

Regimen C: Postoperative Treatment. Enter all patients from Regimen B with residual invasive tumor in the bladder and/or positive nodes and randomize to Arms IV or V. Patients with no tumor in bladder and negative nodes receive no further treatment.

Arm IV: Single-agent Chemotherapy. CACP.

Arm V: No further treatment.

STRATIFICATION BY: Clinical stage (T2B1 vs. T3B2 vs. T3C vs. T4D1), histologic grade (I vs. II vs. III and IV), Karnofsky performance status (60-70 percent vs. 80-100 percent), participating institutions.

SPECIAL STUDY PARAMETERS: Audiogram, IVP, liver scan, bone scan, lymphangiogram, CT scan and ultrasound assessment of retroperitoneum, chest x-ray, tumor measurements, liver size, hematologic parameters, liver and kidney function tests, electrolytes.

END POINTS: Incidence of positive nodes at cystectomy, time to progression, patterns of recurrence, survival, toxicity.

CURRENT STATUS: Patient accrual is anticipated to be about 200 in 4-5 years with an additional 1.5-2 years for follow-up.

DOSAGE SCHEDULE:

Regimen A:

Arm I: 2000 rads total tumor dose megavoltage radiotherapy to the entire pelvis in 5 daily fractions of 400 rads central axis midplane dose during a maximum of 8 days treatment time.

Arm II: CACP - 100 mg/sqm iv infusion over 24 hours on day 1 following prehydration. Radiotherapy as in Arm I, beginning on day 3.

Arm III: Radiotherapy as in Arm I. MNI - 1.5 g/sqm po on days of radiotherapy, 4-6 hours prior to radiotherapy treatment. Arm activated upon availability of MNI.

Regimen B: Total cystectomy and pelvic lymph node dissection between days 21 and 28 of study.

Regimen C:

Arm IV: CACP - 80 mg/sqm iv q month for 6 months.

Arm V: No further treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; MNI - 100 and 500 mg capsules and scored 500 mg enteric coated tablets.

DATE SUMMARIZED: 07/80

3.0004 RADIOTHERAPY WITH NEUTRONS ALONE OR WITH PHOTONS WITH OR WITHOUT SURGERY FOR URINARY BLADDER CANCER

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PROTOCOL NUMBER(S) RTOG-7705

OBJECTIVES:

I. Evaluate the efficacy of, and gather information concerning neutron radiotherapy either alone, in combination with photon radiotherapy, in combination with surgery or in combination with both photon radiotherapy and surgery for urinary bladder cancer, clinical Stage B1, Grade III or IV or clinical Stage B2, C, and D1, any Grade.

II. Determine the morbidity of each treatment.

PROTOCOL ENTRY CRITERIA: Patients under 70 years old with urinary bladder cancer, squamous or transitional cell type, clinical Stage B1 with Grade III or IV histology, or clinical Stage B2, C or D with any histological grade disease. Patients must have a Karnofsky status of 50% or more. Patients may not have had prior pelvic Radiotherapy, prior major pelvic surgery, and may not have para-aortic lymph node involvement with tumor.

PROTOCOL OUTLINE: Nonrandomized study. Institutions choose one or more of the following 4 regimens for Radiotherapy of pelvis and bladder.

Regimen A: Presurgical mixed beam Radiotherapy from x-ray generators with peak photon energy of 4 MeV or greater or Cobalt-60; Neutrons from cyclotron with 21.5 MeV or greater or deuteron energy, or from 14 MeV D-T neutron generator; followed by Cystectomy.

Regimen B: Presurgical Radiotherapy with Neutrons only, followed by Cystectomy.

Regimen C: Mixed beam definitive Radiotherapy. Neutron and photon radiation.

Regimen D: Definitive Radiotherapy with Neutrons only.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Bipedal lymphangiography, urine cytology, small bowel studies, cystourethroscopy.

END POINTS: Response/remission rate, urinary complications or morbidity, G.I. complications or morbidity, tumor progression.

CURRENT STATUS: 40-50 patients will be entered in about 18 months.

DOSAGE SCHEDULE:

Regimen A: Mixed beam Radiotherapy using 2 neutron fractions and 3 photon fractions at 250 rad equivalents to the pelvis 4 times/week for a total of 5000 rad equivalents in 5-6 weeks. A small field boost of 1000 rad to areas shown positive on the lymphangiogram is permitted. Radical cystectomy - performed 4-6 weeks after the conclusion of Radiotherapy.

Regimen B: Radiotherapy using neutrons only - dosage and radical cystectomy as in Regimen A.

Regimen C: Mixed beam Radiotherapy using 2 neutron fractions and 3 photon fractions to the pelvis at 250 rad, 4 times/week for a total of 5000 rad in 5-6 weeks, followed by an additional 6-8 fractions to the bladder using small fields for an estimated total dose of 6500-7000 rad in 6.5-7 weeks.

Regimen D: Radiotherapy using neutrons alone - dosage as in Regimen C.

Follow up all patients monthly during treatment, then q 3-4 months for 2 years, then q 6 months for life.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00050478

3.0005 ADJUVANT RADIOTHERAPY BEFORE AND AFTER SURGERY FOR BLADDER CANCER

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7804

OBJECTIVES:

I. Determine the acceptable postoperative radiation dose following a single preoperative treatment of 500 rad.

II. Determine the morbidity of the combined radiation and surgery in bladder cancer in terms of acute and late tissue reaction and damage.

III. Determine the duration of disease-free survival with adjuvant radiation therapy using a 'sandwich technique.'

IV. Determine the major causes and sites of failure of treatment.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with histologically confirmed transitional or squamous cell carcinoma of the bladder with clinically staged B2 or C lesions. Patients must not have other neoplasms or distant metastases, and must not have had prior pelvic irradiation.

PROTOCOL OUTLINE: Nonrandomized study. Assign all patients to Regimen A, then assign Surgical Stages 0, A, B1 (Grade 1 or 2) to Regimen B and Surgical Stages B1 (Grade 3 or 4) B2, C or D to Regimen C.

Regimen A: Radiotherapy plus Surgery. Supervoltage radiation plus simple or radical cystectomy with urinary diversion.

Regimen B: No further treatment.

Regimen C: Radiotherapy.

STRATIFICATION BY: Clinical stage of disease, participating institutions.

SPECIAL STUDY PARAMETERS: Bone and liver scans, IVP, bipedal lymphangiogram, localizing cystogram.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, disease-free interval, survival time, correlation of lymphangiographic and histological appearance of lymph nodes, morbidity/benefit ratio, correlation of clinical and pathological staging, recurrence sites.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: 500 rads preoperatively to the pelvis in one treatment on the day of or day prior to simple or radical cystectomy with urinary diversion.

Regimen B: No further treatment.

Regimen C: 4500 rad delivered postoperatively in 5 weeks to the target volume.

Follow up all patients q 6 weeks for 3 months, q 3 months through the end of the 2nd year, then q 6 months for life.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 09/78

3.0006 PHOTON RADIOTHERAPY VS PION RADIOTHERAPY FOR TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER

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United States of America

PROTOCOL NUMBER(S) RTOG-7826

OBJECTIVES:

I. Determine whether pi meson (pion) radiotherapy can improve local control and survival in patients with carcinoma of the urinary bladder.

PROTOCOL ENTRY CRITERIA: Patients between the ages of 18 and 75 with biopsy-proven Stage T3 or T4 transitional cell bladder carcinoma who have had no prior definitive therapy. Patients may have no metastases beyond pelvic nodes and must have a Karnofsky performance status of 60 or better plus adequate pulmonary function. Tumor may be locally extensive and nonresectable.

PROTOCOL OUTLINE: Randomized study.

Arm I: Photon Radiotherapy. Co-60 or 4 MeV or greater equipment at parent institution.

Arm II: Pion Radiotherapy. Mesons at Los Alamos Facility.

STRATIFICATION: Participating institutions; histologic grade: low vs. intermediate vs. high; lymphangiogram: positive pelvic nodes vs. negative or equivocal nodes; primary tumor: T3 vs. T4.

SPECIAL STUDY PARAMETERS: Cystogram, IVP, lymphangiogram, cystoscopy, CT scan, cardiopulmonary status evaluation.

END POINTS: Survival time, quality of survival, toxicity/morbidity of treatment, response/remission rate, local recurrence rate, objective tumor response, incidence and response of metastases of regional nodes, incidence of distant metastases.

CURRENT STATUS: 150-200 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Radiotherapy. 6000 rad in 6 to 7 weeks to the bladder, plus 4500 to 5000 rad in 5 to 6 weeks to the pelvis with or without 4500 rad in 5 weeks to the para-aortic area if pelvic nodes are positive.

Arm II: Pion Radiotherapy (Revision September 1979). A minimum of 2000 peak pion rad to the tumor and local lymphatic area plus 1500 rad boost in 15 days to the bladder and pelvis (if nodes are positive) to a maximum total of 4375 peak pion rad. Give additional prophylactic conventional radiotherapy of 4500 rad to the para-aortic area, as in Arm I, if indicated.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

3.0007 PHASE III ADJUVANT CHEMOTHERAPY WITH CTX/ADR/CACP FOR RESECTED TRANSITIONAL CELL BLADDER CARCINOMA

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35294, United States of America

PROTOCOL NUMBER(S) SEG-78BL0103; SEG-78BL339

OBJECTIVES:

I. Determine the effect of adjuvant combination chemotherapy with cyclophosphamide (CTX)/adriamycin (ADR)/cis-platinum (CACP) following preoperative radiotherapy and complete resection for patients with transitional cell carcinoma of the bladder who are at high risk for recurrence.

PROTOCOL ENTRY CRITERIA: Patients with nonmetastasized, transitional cell carcinoma of the bladder whose worst pathological stage (pre- or post-Radiotherapy) is Jewett-Strong B1 with poor prognostic factors, B2, or greater. Patients must have undergone preoperative irradiation, total cystectomy with lymphadenectomy, must have adequate hematologic, liver and renal function. Patients must not have had prior systemic Chemotherapy, prior Radiotherapy for bladder, history of another serious malignancy, and may not have residual disease.

PROTOCOL OUTLINE: Randomized study, following Regimen A.

Regimen A: Radiotherapy plus Surgery. Laparotomy, cystectomy, and lymphadenectomy plus irradiation of tumor and bilateral pelvic lymph nodes.

Arm I: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Arm II: No further therapy.

STRATIFICATION BY: Participating institutions; clinical Stage prior to Radiotherapy: B2 vs. C vs. D; pathologic Stage at resection: O, A, B1 vs. B2, C, D1, D2 with complete resection of nodes vs. D1, D2 with incomplete resection of nodes; tumor grade (Broder): I vs. II vs. III vs. IV.

SPECIAL STUDY PARAMETERS: Cystoscopy and biopsy, lymphangiography, CTX scan or ultrasound, bone and liver scan, SMA-12, carcinoembryonic antigen, audiometry.

END POINTS: Response/remission rate, disease-free interval, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: 220 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Regimen A: Radiotherapy - 1800 to 2300 rads to tumor and bilateral pelvic lymph nodes plus surgery: laparotomy, cystectomy, and lymphadenectomy. Randomize patients within 60 days of completion of Regimen A therapy (Revision November, 1978) to Arms I or II.

Arm I: CTX - 400 mg/sqm (maximum 1000 mg); ADR - 40 mg/sqm (maximum 100 mg); CACP - 60 mg/sqm (maximum 80 mg) with hydration all given iv on day 1 q 4 weeks for 6 courses (Revision November, 1978). Increase dose of CTX and ADR by 25% if there is no Grade 1 toxicity after 2 courses. Remove patients with disease progression after 6 courses from study.

Arm II: No Chemotherapy. Evaluate patients q 4 weeks and crossover patients with disease progression to Arm I.

Observe all patients for survival duration.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; ADR - 10 and 50 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 00080978

3.0008 PHASE III CHEMOTHERAPY WITH CTX/ADR/CACP VS CACP FOLLOWED BY MAINTENANCE OR NO THERAPY FOR METASTATIC BLADDER CARCINOMA

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PROTOCOL NUMBER(S) SEG-79BL351

OBJECTIVES:

I. Compare the response rate of combination chemotherapy with CAP-I: cyclophosphamide (CTX)/adriamycin (ADR)/cis-platinum (CACP) vs. CACP for patients with measurable metastatic carcinoma of the bladder.

II. Determine the efficacy of continuing the same treatment for Maintenance vs. no treatment for patients who respond or are stable after 3 courses of therapy.

PROTOCOL ENTRY CRITERIA: Patients with measurable, inoperable or metastatic (except CNS metastatic disease refractory to radiation therapy and/or steroids), primary carcinoma of the bladder. Patients must have a Karnofsky performance status of at least 40% (or Zubrod scale of at least 3) unless estimated survival is at least 12 weeks; and adequate hematologic, liver and kidney function. Patients must not have been exposed to prior systemic chemotherapy with any of the drugs used in this protocol.

PROTOCOL OUTLINE: Study randomized for Induction and Maintenance.

Induction:

Arm I: 3-Drug Combination Chemotherapy. CAP-I: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Arm II: Single-agent Chemotherapy. CACP.

Maintenance:

Randomize patients with stable, partial or complete response to continued induction therapy or to no further therapy.

Arm III: 3-Drug Combination Chemotherapy or Single-agent Chemotherapy. Continue Induction therapy on Arm I or Arm II.

Arm IV: No further therapy.

STRATIFICATION: Histological type and grade, performance status; participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, liver and kidney function; SMA-12; ultrasound and CAT scans and/or x-rays; audiometry.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 75 patients per year will be entered for 3 years.

DOSAGE SCHEDULE:

Arm I: CAP-I: CTX - 400 mg/sqm (1000 mg maximum); ADR - 40 mg/sqm (100 mg maximum); CACP - 60 mg/sqm (120 mg maximum) with adequate intravenous hydration; all given iv on day 1 q 3 weeks for 3 courses.

Arm II: CACP - as in Arm I.

Remove from study patients with disease progression.

Maintenance:

Arm III: Continue Induction, Arm I or II, q 4 weeks for 8 courses or until disease recurrence.

Arm IV: No further treatment. Retreat patients who progress on no treatment with 8 courses of initial induction therapy or until disease progression. Remove patients with disease progression from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; ADR - 10 and 50 mg vials; CACP - 10 and 25 mg vials.

DATE SUMMARIZED: 11/79

3.0009 PHASE II-III HMM VS FAC (5-FU/ADR/CTX) CHEMOTHERAPY FOR ADVANCED TRANSITIONAL CELL BLADDER CANCER WITH IMPAIRED RENAL FUNCTION

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PROTOCOL NUMBER(S) SWOG-7904

OBJECTIVES:

I. Compare the efficacy (response rate) of hexamethylmelamine (HMM) versus FAC: 5-fluorouracil (5-FU), adriamycin (ADR), and cyclophosphamide (CTX) in locally recurrent or disseminated transitional cell bladder carcinoma, in patients with impaired renal function, with crossover upon treatment failure.

PROTOCOL ENTRY CRITERIA: Patients with measurable disease no longer amenable to surgery or radiotherapy with histologically proven T4 transitional cell bladder cancer, with recurrent or residual disease and/or with M1 liver, osseous, pulmonary or other metastases. Patients must not have had prior chemotherapy and must have concluded prior radiotherapy 3 weeks before study entry. They must have adequate hematologic and cardiac function and adequate bilirubin and creatinine clearance values. Poor-risk entries (PRP) are patients over 65 years of age, or who have had prior pelvic radiotherapy or a creatinine clearance less than 50 cc/min.

PROTOCOL OUTLINE: Randomized study, with crossover upon treatment failure.

Arm I: 3-Drug Combination Chemotherapy. FAC - 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm II: Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

STRATIFICATION BY: Good- vs. poor-risk patients.

SPECIAL STUDY PARAMETERS: Liver and bone scan; CAT scan of pelvis; pelvic sonography; optional: IVP and lymphangiogram.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, response duration, survival time.

CURRENT STATUS: 120 patients will be entered in 2 to 2.5 years.

DOSAGE SCHEDULE:

Arm I: 5-FU - 400 mg/sqm (300 mg/sqm for PRP, maximum dose 1 g) iv on days 1 and 8; ADR - 40 mg/sqm (30 mg/sqm for PRP, maximum cumulative dose 450 mg/sqm) iv on day 1; CTX - 400 mg/sqm (300 mg/sqm for PRP) iv on day 1. Repeat course q 3 weeks.

Arm II: HMM - 320 mg/sqm/day (240 mg/sqm/day for PRP) given po in 4 divided doses for 21 days q 6 weeks if hematological recovery has occurred.

Consider 1 course in either arm an adequate trial. Cross over patients failing to respond or relapsing after initial response to alternate arm. Remove from study patients not tolerating the lowest dose levels of both treatments and patients with progressive or unsatisfactory stable disease after crossover therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules; 5-FU - 500 mg ampules; CTX - 100 and 500 mg ampules; HMM - 50 and 100 mg capsules.

DATE SUMMARIZED: 06/79

3.0010 PHASE II-III CHEMOTHERAPY WITH CAP-I (CTX/ADR/CACP) VS AMSA FOR ADVANCED TRANSITIONAL CELL CANCER OF THE URINARY BLADDER

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7922

OBJECTIVES:

I. Compare effects of CAP-I: cyclophosphamide (CTX)/adriamycin (ADR)/cis-platinum (CACP) vs. AMSA for patients with good renal function who have advanced, transitional cell carcinoma of the urinary bladder and have failed on previous surgery and/or radiotherapy.

II. Determine response rate to alternate treatment arm following cross-over of patients failing initial therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, Stage IV transitional cell carcinoma of the urinary bladder who have failed on previous surgery and/or radiotherapy. Patients must have life expectancy of at least 8 weeks, good renal function, at least 1 functioning kidney, and adequate hematologic and liver function. Patients must not have received prior systemic chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. CAP-I: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Arm II: Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: Participating institutions; risk: good vs. poor.

SPECIAL STUDY PARAMETERS: IVP or renal scan, bilateral audiogram.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 40 patients per year will be entered.

DOSAGE SCHEDULE: Good-risk patients are not above 65 years old, have had no prior extensive pelvic radiotherapy, and have a performance status of at least 2. Poor-risk patients (PRP) are over 65 years of age, and/or have had prior extensive pelvic radiotherapy, and/or have a performance status greater than 2, and/or have poor bone marrow reserve.

Arm I: CAP-I: CTX - 600 mg/sqm (500 mg/sqm for PRP) iv bolus with adequate prior hydration on day 1; ADR - 50 mg/sqm (40 mg/sqm for PRP) iv bolus on day 1; CACP - 75 mg/sqm iv on day 2 with adequate mannitol diuresis and hydration. Give Allopurinol - 300 mg/day po with CAP-I therapy. Repeat course q 3 to 4 weeks if patient maintains adequate hematologic and kidney function.

Arm II: AMSA - 120 mg/sqm (100 mg/sqm for PRP) iv 30 to 60 min infusion in 250 cc D5W q 3 weeks if patient has adequate hematologic and liver functions.

Cross over to alternate treatment arm patients who respond and subsequently relapse, show increasing disease after 1 or more courses, or have clinically unsatisfactory stable disease after 2 or more courses. Enter patients who develop Grade 3 hematologic toxicity to PRP dosages of crossover arm.

Remove from study patients with disease progression after 1 or more courses or clinically unsatisfactory stable disease after 2 or more courses of both original and crossover treatment arms, and patients who fail on original arm and do not qualify for crossover arm. Those with unacceptable toxicity, severe hepatic dysfunction, congestive heart failure, or moderate to severe renal toxicity are also removed from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg ampules; ADR - 10 and 50 mg vials; CACP - 25 or 10 mg vials; AMSA - 75 mg ampules.

DATE SUMMARIZED: 11/79

3.0011 CHEMOTHERAPY WITH HMM FOR METASTATIC TRANSITIONAL-CELL CARCINOMA OF THE BLADDER

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PROTOCOL NUMBER(S) UORG-06

OBJECTIVES:

I. Determine the efficacy of hexamethylmelamine (HMM) in patients with advanced transitional-cell carcinoma of the bladder.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed measurable or evaluable metastatic transitional-cell carcinoma of the bladder. Patients must have a wbc less than 2500, a platelet count less than 150,000, a creatinine clearance of 50 cc/mm or a serum creatinine less than 2.5 mg%. Patients must have a life expectancy of at least 2 months, and must not have received any chemotherapy within the 2 weeks prior to entry. Patients who have received prior chemotherapy with the study agents are not eligible.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Kidney and liver function tests.

END POINTS: Toxicity/morbidity of treatment, objective tumor response rate, duration of response, quality of response.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

HMM - 10 mg/kg/day orally in 4 divided doses after meals and at bedtime for 21 days, followed by a 4-week rest period. Repeat course for a minimum of 2 until no response, objective evidence of progression, or unacceptable toxicity is documented.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/78

3.0012 CHEMOTHERAPY WITH INTRAVESICAL MITOMYCIN-C FOR SUPERFICIAL URINARY BLADDER TUMORS (STAGES O/A)

Johnson, D. E., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-163

OBJECTIVES:

I. Determine the efficacy of intravesical instillations of mitomycin-C in eradicating low-grade, low-stage (Stage O/A) transitional-cell carcinomas of the urinary bladder.

PROTOCOL ENTRY CRITERIA: Patients with recent histologically proven transitional cell carcinomas of the urinary bladder whose malignant lesions are confined to the mucosa or lamina propria (Stages O/A) and with superficial tumors in which endoscopic excision is impossible. Patients with extension of the malignant process into the muscular wall or beyond, with a platelet count less than 150, 000, with wbc less than 4,000, with serum creatinine greater than 3 mg %, or who receive other antineoplastic systemic agents are excluded from the study.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, objective tumor response.

CURRENT STATUS: 28 patients will be entered over 2 years.

DOSAGE SCHEDULE:

MITO - 25 mg intravesicularly once a week for a maximum of 8 doses. At 12 weeks, repeat cystoscopy to evaluate response. If response is observed, subsequent treatment is: MITO - 25 mg, monthly (number of treatments is at discretion of investigator). Continue cystoscopy every 3 months for 1 year. If no response is detected, either discontinue or increase the dose by 5-mg increments in a repeat regimen of weekly therapy.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 01/77

3.0013 ADJUVANT CHEMOTHERAPY WITH ADRIAMYCIN FOLLOWING RADIOTHERAPY AND CYSTECTOMY FOR INFILTRATING CARCINOMA OF THE BLADDER

Bracken, R. B., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-219

OBJECTIVES:

I. Evaluate the efficacy of adjuvant chemotherapy with ADR for improving survival rates for patients undergoing preoperative radiotherapy and cystectomy for invasive bladder carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with transitional carcinoma of the bladder clinical Stage B2 or C.

PROTOCOL OUTLINE: Randomized study.

Following preoperative Radiotherapy and Cystectomy, randomize patients to Arm I or Arm II.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: No Chemotherapy.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, survival rate, disease free interval, length of survival.

CURRENT STATUS: 152 patients will be entered in about 5 years.

DOSAGE SCHEDULE:

Arm I: ADR - 50 mg/sqm (route not given). Repeat q 3 weeks for a total of 6 courses.

Arm II: No therapy.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/78

3.0014 INTRAVESICAL CHEMOTHERAPY WITH THIOTEPA VS MITOMYCIN-C FOR NON-INVASIVE TRANSITIONAL BLADDER CARCINOMA

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PROTOCOL NUMBER(S) MDAR-347; MDA-U/u27

OBJECTIVES:

I. Compare the efficacy of intravesicular chemotherapy with thiotepa vs. mitomycin-C for non-invasive transitional cell carcinoma of the urinary bladder.

PROTOCOL ENTRY CRITERIA: Patients with recent, histologically confirmed, transitional cell carcinoma of the urinary bladder confined to the mucosa or lamina propria. Tumors must be superficial and not amenable to endoscopic excision. Patients must have a life expectancy of at least 9 months, and adequate hematologic, kidney, and bladder function. Patients must not have received more than 2000 rad pelvic irradiation or prior treatment with protocol drugs.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Thiotepa, NSC-6393.

Arm II: Single-agent Chemotherapy. Mitomycin-C, MITO, NSC-26980.

STRATIFICATION: Participating institutions; histology: papillary vs. flat in situ cancer.

SPECIAL STUDY PARAMETERS: Cystoscopy.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, survival rate.

CURRENT STATUS: 250 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Thiotepa - 60 mg in 60 ml water instilled via catheter into the urinary bladder and retained (if possible) for 2 hours q 7 days for 4 weeks.

Arm II: MITO - 40 mg in 40 ml water instilled into the bladder as in Arm I q 7 days for 8 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

3.0015 BCG PLUS FULGURATION VS FULGURATION ALONE FOR RECURRENT MULTICENTRIC SUPERFICIAL BLADDER CANCER

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PROTOCOL NUMBER(S) MSKCC-7766

OBJECTIVES:

I. Decrease the recurrence rate of superficial bladder cancer by the use of intravesicular and percutaneous BCG.

PROTOCOL ENTRY CRITERIA: Patients with multicentric (in time and/or space) bladder tumors, including patients with Jewett's Stages O, A, and low grade B-1 disease as well as patients with recurrent papilloma.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery. Transurethral resection and electrocoagulation.

Arm II: Surgery plus Immunotherapy. Fulguration as in Arm I plus BCG-unspecified, no NSC# given.

STRATIFICATION BY: Disease histology: papilloma vs. superficial cancer.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Recurrence rate.

CURRENT STATUS: Entry of 34 patients in each arm will produce statistically valid results.

DOSAGE SCHEDULE:

Arm I: Surgery.

Arm II: BCG - 120 mg in 50 ml intravesicularly, retained for 2 hours, and 5 x 10 to the seventh viable units percutaneously by the multiple tine technique, q week for 6 weeks after fulguration.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/80

3.0016 ADJUVANT IMMUNOTHERAPY WITH BCG FOR BLADDER CANCER

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PROTOCOL NUMBER(S) MI-BL-1

OBJECTIVES:

I. Determine whether adjuvant immunotherapy with BCG will improve the remission rates, survival times, and cure rates of patients with a history of recurrent superficial bladder cancer.

PROTOCOL ENTRY CRITERIA: Patients who have had two or more recurrences of superficial bladder cancer without known metastatic spread.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. Tice BCG, BCG, NSC-B116327.

Arm II: No Immunotherapy.

STRATIFICATION BY: Participating institutions; staging by the American Joint Committee.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients are to be entered.

DOSAGE SCHEDULE:

Arm I: A single multiple-puncture tine technique vaccination will be given at two sites the first week. Beginning one week later, BCG will be administered intravesically by forcibly instilling one ampule of BCG (5 x 10 to the eighth organisms) in 50 ml of sterile water to be retained by the patient for two hours under observation. This intravesical instillation will be repeated weekly, for a total of six instillations and then monthly for one year.

Arm II: No Immunotherapy with BCG.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 2-8 x 10 to the eighth colony-forming units per ampule.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

3.0017 IMMUNOTHERAPY WITH INTRAVESICULAR AND PERCUTANEOUS BCG ADJUVANT TO SURGERY IN RECURRENT SUPERFICIAL BLADDER CANCER

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Texas, 78284, United States of America
PROTOCOL NUMBER(S) TX-UTHSC-BL-1

OBJECTIVES:

I. Evaluate the therapeutic efficacy of intravesicular and percutaneous BCG in patients with recurrent bladder cancer.

PROTOCOL ENTRY CRITERIA: All patients with Stage O, A, or B transitional cell carcinoma of the bladder who are not candidates for cystectomy. Diagnosis to entry interval must be less than 3 years.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery. Standard surgical therapy alone.

Arm II: Surgery plus Immunotherapy. Standard surgical therapy; BCG-Pasteur, BCG, NSC-B116328.

STRATIFICATION BY: One vs. two or more tumor recurrences in the previous year; Grade I vs. Grade II or more.

SPECIAL STUDY PARAMETERS: Cellular in vitro immunity to bladder tumor antigens and PPD, skin tests.

END POINTS: Recurrence rate and disease-free interval.

CURRENT STATUS: 51 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: Standard surgical therapy.

Arm II: Surgery as in Arm I. BCG - 120 mg in 50 cc normal saline, intravesicularly, each week for six weeks; BCG - 5 mg, percutaneously (Heaf gun) to alternate upper thighs, each week for six weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 40 and 120 mg vials.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 00510280

3.0018 INTRAVESICULAR ADR FOLLOWING TRANSURETHRAL RESECTION FOR NONMETASTATIC BLADDER WALL PAPILLARY CARCINOMA

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PROTOCOL NUMBER(S) BRA-LACRIP-031

OBJECTIVES:

I. Evaluate intravesicular adriamycin following transurethral resection in patients with T1 and Tis papillary carcinoma of the bladder wall.

II. Determine local and systemic toxicity of treatment.

PROTOCOL ENTRY CRITERIA: Patients with T1 and Tis papillary carcinomas of the bladder wall who have undergone transurethral resection, preferably 30 days earlier. Fulguration may have been performed for small papillomas localized in the anterior wall of the vault of the bladder. Patients may not have had prior adriamycin therapy and may not have had chemotherapy or local radiotherapy within the prior 3 months. Patients must have adequate renal function and may not have untreated or refractory urinary tract infections.

PROTOCOL OUTLINE: Nonrandomized study. All patients undergo transurethral resection of tumor with or without fulguration of papillomas prior to initiation of local Chemotherapy.

Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Cytoscopy, renal and hepatic function tests, electrocardiogram, excretory urography, urethrocystography, polycystography, chest films, hepatic scintiscan, hematologic parameters.

END POINTS: Incidence of relapse, disease-free interval, toxicity of treatment.

CURRENT STATUS: Not specified.

DOSAGE SCHEDULE:

ADR - 80 mg in 80 ml of sterile distilled water intravesicularly for 60 minutes repeated weekly for 4 weeks then q 4 weeks for a total of 15 instillations.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/80

3.0019 PHASE III VITAMIN THERAPY WITH PYRIDOXINE FOR RESECTED TRANSITIONAL CELL TUMORS OF THE BLADDER

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Cancer, Genito-Urinary Tract Cancer Coop. Grp., General
Infirmary, Pontefract, West Yorkshire, United Kingdom
PROTOCOL NUMBER(S) EORTC-30781

OBJECTIVES:

I. Determine the incidence of abnormal tryptophan metabolites in the urine of patients with Ta and T1 category transitional cell tumors of the bladder.

II. Determine whether the oral administration of pyridoxine decreases the rate of recurrence of Ta and T1 bladder tumors in patients with abnormal tryptophan metabolites in the urine or in patients with normal tryptophan metabolites in the urine.

PROTOCOL ENTRY CRITERIA: Patients with Ta and T1 NXMX and Ta and T1 N0M0 transitional cell bladder tumors that can be completely destroyed by a transurethral resection or fulgurization. Patients must have a life expectancy greater than 3 years and be medically fit for repeated cystoscopy. Patients must have no other neoplasm (except non-melanomatous skin cancer) and no history of overt psychiatric disorder. Patients may have received no previous treatment for bladder tumors other than transurethral resection or fulgurization and may receive no current treatment with para-amino salicylic acid, oestrogens, sulphonamides, or isoniazid.

PROTOCOL OUTLINE: Randomized study. Double blind. Patients are randomized following transurethral resection or fulgurization.

Arm I: Single-agent Chemotherapy. Pyridoxine, VIT-B6, NSC-36225.

Arm II: Placebo.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tryptophan load test, cystoscopy, red cell ASP-T and PALP, I.V.P.

END POINTS: Time interval until first recurrence, tumor recurrence rate, number of tumors present at each cystoscopy, change in the T or G category.

CURRENT STATUS: 134 patients have been entered as of May 1980. A total of 152 patients will be entered and followed until first recurrence.

DOSAGE SCHEDULE:

Patients begin therapy within 7-14 days of Surgery.

Arm I: VIT-B6 - 20 mg per day.

Arm II: Placebo.

Treatment will be continued until the conclusion of the study; upon recurrence all tumors will be completely resected or fulgurized. Patients go off study when recurrent tumors cannot be controlled by transurethral resection or there is a change in the T, M, N, or G category.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

3.0020 PHASE III CHEMOTHERAPY WITH THIOTEPA OR CACP OR ADR FOR RECURRENT RESECTABLE TA OR T1 PAPILLARY CARCINOMA OF THE BLADDER

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PROTOCOL NUMBER(S) EORTC-30782

OBJECTIVES:

I. Compare in patients with recurrent transitional cell bladder tumors (category Ta or T1) after complete destruction of all visible tumor by transurethral resection, (a) the duration of the disease-free interval, (b) the recurrence rate (including an evaluation of the number and size of recurrent tumors), and (c) the percentage of patients with an increase in the G or T category after intravesical administration of thiotepa, adriamycin, or cis-platinum.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven, recurrent, resectable, category Ta or T1 papillary transitional cell carcinoma of the bladder. Patients must have had a transurethral resection of the lesion, including a deep biopsy of the underlying bladder wall, and have no visible lesions. Patients must be expected to survive the duration of the study and have adequate hematologic, renal and cardiac function. Patients must have no urethral stricture precluding repeated endoscopic resection, psychosis, senility, untreated urinary tract infection, or other cancer type. Patients must have no previous chemotherapy with the protocol agents and no chemotherapy/radiotherapy within 3 months of entry.

PROTOCOL OUTLINE: Randomized study. Patients are randomized following transurethral resection. Patients with recurrence during Chemotherapy undergo a second resection.

Arm I: Single-agent Chemotherapy. Thiotepa, NSC-6396.

Arm II: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm III: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions, interval between resection and chemotherapy.

SPECIAL STUDY PARAMETERS: Cystoscopy, biopsy of urethelium, WBC and platelets, blood urea, serum creatinine.

END POINTS: Disease-free interval, number and size of recurrences, presence of urethelial abnormalities, increase in T or G categories.

CURRENT STATUS: 115 patients have been entered as of June 1980. A total of 228 evaluable patients will be entered and followed until first recurrence.

DOSAGE SCHEDULE:

Treatment begins 24 hours-14 days after transurethral resection; for analysis, patients are allocated in 2 groups on the basis of this interval between resection and chemotherapy (24 hours to 4 days and 10 days to 14 days).

Arm I: Thiotepa - 50 mg in 50 ml of distilled water, instilled into the bladder and retained for one hour, and repeated q week for 4 weeks, then q 4 weeks for 11 instillations (15 total instillations). Drug-induced hematologic, cardiac or renal toxicity or bacterial cystitis will delay the next instillation.

Arm II: ADR - 50 mg in 50 ml of distilled water administered as in Arm I.

Arm III: CACP - 50 mg in 50 ml of distilled water administered as in Arm I.

Upon recurrence, transurethral resection is performed and Chemotherapy is restarted and continued for one year after the first resection. Patients who develop drug-induced cystitis or toxicity that cannot be controlled go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Thiotepa - 10 and 15 mg vials or 100 ml bottles; ADR - 10 and 50 mg ampules; CACP - 10 mg vials.

DATE SUMMARIZED: 10/80

3.0021 PHASE III CHEMOTHERAPY WITH ADR/5-FU FOLLOWING RADICAL CYSTECTOMY WITH OR WITHOUT RADIOTHERAPY FOR CARCINOMA OF THE BLADDER

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PROTOCOL NUMBER(S) EORTC-30784

OBJECTIVES:

I. Compare the disease-free interval in 2 groups of patients with P3 category, N- or N1,2 and M0 transitional cell carcinoma of the bladder treated primarily by radical cystectomy, where one group receives postoperative chemotherapy with adriamycin and 5-fluorouracil and the other group receives no postoperative treatment.

PROTOCOL ENTRY CRITERIA: Patients with clinical T3,M0 category transitional cell carcinoma of the bladder; the pathological examination of the radical cystectomy specimen must reveal muscular invasion (PT2,PT3) and the regional nodes must be either free of disease or involved (PN0,PN1,PN2,PN3), irrespective of the number of the affected nodes found below the mid-portion of the common iliac vessels. Patients must be under 70 years of age and have a performance scale (ECOG) status of 0, 1 or 2. Patients must have adequate hematologic, renal, cardiac and hepatic function. Patients must have no additional neoplasms (except skin nonmelanoma) and no uncontrollable urinary tract infection, psychiatric disorders or untreatable chronic disease. Patients must have no previous major surgery, radiotherapy, or chemotherapy other than intravesical topic chemotherapy.

PROTOCOL OUTLINE: Patients are randomized to Arms I and II following treatment in Regimen A or in Regimen B. Each participating center should choose either Regimen A or Regimen B for all their patients; no crossover (of Radiotherapy) will be allowed.

Regimen A: Preoperative Radiotherapy plus Surgery. Whole pelvis irradiation plus radical total cystectomy.

Regimen B: Surgery. Radical cystectomy.

Arm I: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; plus 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: No further treatment.

STRATIFICATION BY: Radiotherapy vs. no radiotherapy; grade: G1 vs. G2,G3; invasion: PT2 vs. PT3; nodal status: PN0 vs. PN1,2,3.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; chest x-ray; I.V.P.; bone scan; liver scan; laparoscopy; immunological profile; biological cancer markers.

END POINTS: Disease-free interval, survival rates, toxicity of treatment.

CURRENT STATUS: 24 patients have been entered as of June 1980. A total of 152 patients will be entered and followed until relapse.

DOSAGE SCHEDULE:

Regimen A: Co-60 or x-ray generators producing beams with peak photon energy of 2 MeV or greater - 1500 rads depth dose calculated to the midpoint of the pelvic volumen in two 750-rad fractions in 2 days. Between 2 and 5 days following irradiation, a radical total cystectomy is performed; the regional lymph nodes up to the mid portion of the common iliac vessels should be excised. For men with prostatic-urethral invasion, urethrectomy is performed; for women, a routine urethrectomy is recommended.

Regimen B: Surgery as in Regimen A.

Arm I: Chemotherapy begins within 2 months following cystectomy. ADR - 40 mg/sqm iv in a fast running infusion of 5 percent dextrose on day 1; 5-FU - 500 mg/sqm iv bolus or im on days 2, 3, 4 of week 1; 5-FU - 300 mg/sqm im on day 1 of weeks 2, 3 and 4. Course is repeated q month for 1 year or until a total dose of 500 mg/sqm of ADR is completed.

Arm II: Followup and observation. Patients may cross over to Arm I when disease recurs.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

3.0022 PHASE III CHEMOTHERAPY WITH ADR OR EPODYL FOR RESECTED T1 AND TA PAPILLARY CARCINOMA OF THE BLADDER

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PROTOCOL NUMBER(S) EORTC-30790

OBJECTIVES:

I. Compare the disease-free interval after transurethral resection (TUR) only and TUR followed by chemotherapy with either local adriamycin or epodyl.

II. Compare the stage of malignancy of recurrent tumor and the frequency and multiplicity of recurrent tumors after the described treatment.

PROTOCOL ENTRY CRITERIA: Patients with primary or recurrent resectable Ta and T1 papillary carcinoma of the bladder. Patients must undergo transurethral resection including a deep biopsy of the underlying bladder wall; all visible lesions must be completely destroyed. Patients will be expected to survive the duration of the study and must have adequate hematologic and cardiac function. Patients must have no overt psychosis, recurrent severe drug-induced cystitis or another cancer type other than transitional cell carcinoma. Patients must have had no open surgery within 3 months of entry, no chemotherapy within 3 months of entry and no radiotherapy within 12 months of entry. Patients must have received no previous treatment with the protocol agents.

PROTOCOL OUTLINE: Randomized study. Patients are randomized following TUR.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: Single-agent Chemotherapy. Epodyl, NSC-80439.

Arm III: No treatment.

STRATIFICATION BY: Primary disease vs. recurrent disease.

SPECIAL STUDY PARAMETERS: Cystoscopy, biopsy, hematologic and renal function tests.

END POINTS: Disease-free interval, number and size of recurrences, presence of other urethelial abnormalities, increase in T or G categories.

CURRENT STATUS: 33 patients have been entered as of June 1980. A total of 228 evaluable patients will be entered and followed until recurrence.

DOSAGE SCHEDULE:

Treatment begins no later than 1 week after TUR.

Arm I: ADR - 50 mg in 50 ml normal saline is instilled into the bladder (via a urethral catheter) and remains in the bladder for 1 hour, q week for 4 weeks then q 4 weeks for 11 instillations (15 total). Nitrofurantoin will be given after each instillation - 300 mg a day for 3 days. The presence of hematologic toxicity or cystitis will delay drug administration.

Arm II: Epodyl - 1.13 g in 100 ml of distilled water is instilled via a urethral catheter into the bladder on the same schedule as per Arm I.

Arm III: No treatment.

Treatment continues for 1 year, and patients are followed for 5 years or until death or recurrence.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 50 mg vials; Epodyl - 1.13 g vials.

DATE SUMMARIZED: 10/80

3.0023 PHASE II CHEMOTHERAPY WITH VINCRISTINE FOR ADVANCED CARCINOMA OF THE BLADDER

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PROTOCOL NUMBER(S) EORTC-30797

OBJECTIVES:

I. Evaluate the activity of vincristine in advanced bladder cancer with respect to objective tumor response rate and the duration of any response.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven transitional cell carcinoma of the bladder (all N, M, P, G, and L classifications and T1 and T2 categories with measurable metastatic disease), with measurable primary or metastatic disease that is progressing despite therapy. Patients must be under 80 years of age, have an estimated survival time of at least 90 days, a performance status (ECOG) of 0, 1, or 2, and must be free from infection of the urinary tract. Patients must not have another neoplasm (except skin non-melanoma), psychiatric disorders, or senility. Patients must have no previous chemotherapy with vincristine or radiotherapy to the indicator lesion.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; chest x-ray; cystoscopy; E.U.A.; biopsy; liver scan; bone survey; I.V.P.

END POINTS: Response rate, objective tumor response, duration of response, toxicity of treatment, duration of survival.

CURRENT STATUS: 21 patients have been entered as of June 1980; 29 patients will be entered. If 3 or fewer responses are obtained, the drug will be rejected.

DOSAGE SCHEDULE:

VCR - 1 mg/sqm iv q week for 8 weeks (VCR maximum dose is 2 mg). Treatment continues until progression of disease or neurological toxicity occurs. Patients with stable disease or objective response at the end of 8 weeks continue on the same dose q 2 weeks until progression or toxicity develops.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

3.0024 ADJUVANT CHEMOTHERAPY WITH ADRIAMYCIN/5-FLUOROURACIL FOLLOWING RADICAL RADIOTHERAPY FOR T3, NX, M0 BLADDER CARCINOMA

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PROTOCOL NUMBER(S) UICC-78025; UKM-YUCRG-771

OBJECTIVES:

I. Assess the effect of adjuvant chemotherapy with adriamycin (ADR) and 5-fluorouracil (5-FU) after high-energy radiation (HER) for T3 bladder cancer.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with newly diagnosed, T3M0 transitional cell carcinoma of the bladder. Patient may not have another neoplasm.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy.

Arm II: Radiotherapy plus 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Participating institutions, histological tumor grade.

SPECIAL STUDY PARAMETERS: Bone scan, LFT.

END POINTS: Response rate, disease-free interval, persistence of tumor at 6 months after radiotherapy, survival.

CURRENT STATUS: About 150 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Radical Radiotherapy - no details given.

Arm II: Radiotherapy, no details given, plus ADR - 50 mg/sqm iv q 21 days; 5-FU - 500 mg/sqm iv q 21 days. Give a total of 4 to 11 courses.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules; 5-FU - 500 mg vials.

DATE SUMMARIZED: 06/79

PATIENT ACCRUAL: 00770379

3.0025 IMMUNOTHERAPY WITH TUMOR-IMMUNE PIG LYMPH NODE CELLS PLUS RADIOTHERAPY VS RADIOTHERAPY ALONE FOR URINARY BLADDER CANCER

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PROTOCOL NUMBER(S) UKM-BL-1

OBJECTIVES:

I. Determine whether the administration of tumor-immune pig cells followed by an attenuated course of radiotherapy has a greater antitumor effect than administration of radical radiotherapy alone.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven invasive transitional cell carcinoma of the urinary bladder. Patients must be under 70 years of age and have a pelvic mass palpable on bi-manual examination.

PROTOCOL OUTLINE: Randomized study. Similar patients are randomly assigned to two treatment groups.

Arm I: Immunotherapy plus Radiotherapy. Tumor-immune pig lymph node cells; plus 8 MeV linear accelerator irradiation.

Arm II: Radiotherapy. 8 MeV linear accelerator irradiation.

STRATIFICATION BY: Sex; age: below 60 vs. over 60 years of age.

SPECIAL STUDY PARAMETERS: Excretion urography, cystoscopy, bi-manual examination, biopsy, bladder scan.

END POINTS: Response/remission rate, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 35 patients will be added per year, during the 3-year study.

DOSAGE SCHEDULE:

Arm I: Tumor-immune pig lymph node cells - 3 x 10 to the 9th viable cells via a catheter inserted into the arterial blood supply of the tumor. After a 6-week interval, 8 MeV linear accelerator - 4,000 rads to the tumor volume in 15 equal daily fractions over a 3-week period.

Arm II: 8 MeV linear accelerator - 5,500 rads to the tumor volume in 25 daily fractions over a period of 5 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 10/80

3.0026 SINGLE-AGENT CHEMOTHERAPY WITH VM-26 VS CHEMO/IMMUNOTHERAPY WITH VM-26, LEVAMISOL IN RESIDUAL DETECTABLE URINARY BLADDER CANCER

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PROTOCOL NUMBER(S) URU-BL-1

OBJECTIVES:

I. Compare single-agent chemotherapy, VM-26, with combined chemotherapy and immunotherapy, VM-26 plus levamisol, in residual detectable urinary bladder cancer.

II. Evaluate remission response and survival in patients on these two regimens.

PROTOCOL ENTRY CRITERIA: Patients age 70 or younger with histologic diagnosis of carcinoma of the bladder in various grades of differentiation, with TNM classification of lesion. Their minimum hemogram should be: rbc 3 million, wbc 4000, and platelet 100,000/cumm. Patients must have received no prior chemotherapy or immunotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. VM-26, NSC-122819.

Arm II: Single-agent Chemotherapy plus Immunotherapy. VM-26 plus Levamisole, LEV, NSC-177023.

STRATIFICATION BY: Age, blood counts, disease stage.

SPECIAL STUDY PARAMETERS: Hemogram with platelet count, blood nitrogen level, hepatocytic function with transaminases, urine sediment on fourth day of drug administration and before following series. Quarterly: cystoscopy, skin and immunological tests, hepatic gammagram and thorax x-ray.

END POINTS: Response/remission rate; survival rate.

CURRENT STATUS: Five evaluable patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: VM-26 - 35 mg/sqm iv in 250 ml of isotonic serum with glucose for 5 consecutive days per month. If at the end of 12 monthly series a partial regression or greater has not been achieved the patient will be withdrawn from the protocol. Otherwise treatment is continued until relapse.

Arm II: VM-26 as in Arm I, plus LEV - 150 mg/day (3 doses of 50 mg each for 7 days, starting on the 15th day after initiation of VM-26. For patients with body surface of less than 1.2 sqm, the doses are reduced to 100 mg/day.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VM-26 - 50 mg vials; LEV - 50 mg drops.

DATE SUMMARIZED: 02/80

3.0027 COMPARISON OF ADJUVANT CHEMOTHERAPY WITH VM-26 AND ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE FOR NONDETECTABLE CARCINOMA OF THE BLADDER

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PROTOCOL NUMBER(S) URU-BL-2

OBJECTIVES:

I. Obtain increased survival and delay relapse, using chemotherapy with VM-26 or immunotherapy with levamisole (LEV) as adjuvants to curative surgery and/or radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients with carcinoma of the bladder submitted to curative surgery and/or radiotherapy. Patients must be less than 75 years of age, with no previous chemotherapy or immunotherapy, and with no renal, hepatic or hematopoietic insufficiency.

PROTOCOL OUTLINE: Randomized study.

Arm I: No therapy.

Arm II: Single-agent Chemotherapy. VM-26, NSC-122819.

Arm III: Single-agent Immunotherapy. Levamisole, LEV, NSC-177023.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Skin tests for recall antigens, evaluation of extension of disease.

END POINTS: Interval between onset of treatment and clinically detectable evidence of relapse or distant metastases.

CURRENT STATUS: 6 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: No therapy.

Arm II: VM-26 - 35 mg/sqm iv in isotonic dextrose solution (5 percent), 5 days a month for 6 months.

Arm III: LEV - 150 mg/day po, 7 days a month for 6 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: VM-26 - 50 mg vials; LEV - 50 mg capsules.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

3B. KIDNEY

3.0028 PHASE II CHEMOTHERAPY WITH VBL/CCNU/HU AND HORMONE THERAPY WITH MEDROXYPROGESTERONE ACETATE FOR METASTATIC RENAL ADENOCARCINOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-GU-P33

OBJECTIVES:

I. Determine the objective response rate, toxicity, duration of response and effect on survival of the combination therapy with vinblastine (VBL), CCNU, hydroxyurea (HU) and medroxyprogesterone acetate.

PROTOCOL ENTRY CRITERIA: Patients with histological proof or classic appearance on renal arteriogram of measurable metastatic renal adenocarcinoma. Patients must have a Karnofsky performance status of at least 40% and a life expectancy of 3 months. There must have been no prior treatment with the study drugs.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. Vinblastine, VBL, NSC-67574; CCNU, NSC-79037; Hydroxyurea, HU, NSC-32065; and Medroxyprogesterone acetate, MPA, NSC-026386.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: SMA-12, tumor measurements.

END POINTS: Response/rate of remission, objective tumor response, toxicity/morbidity of treatment, duration of response, survival rate.

CURRENT STATUS: About 29 patients will be entered.

DOSAGE SCHEDULE:

Each course lasts 28 days. VBL - 5 mg/sqm iv on day 1; CCNU - 60 mg/sqm po on day 2; HU - 800 mg/sqm/day in 2 divided doses on days 3 through 14; MPA - 1 gm im on day 1 and q 7 days thereafter. Repeat course q 28 days unless development of a new tumor or a 50% increase in measurable disease is observed. Continue patients with objective response or stable disease until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VBL - 5 and 10 mg vials; CCNU - 10, 40 and 100 mg capsules, and 50 mg vials; HU - 500 mg capsules; MPA - 1 g vials and 10 mg tablets.

DATE SUMMARIZED: 07/79

3.0029 PHASE II POSTINFARCTION NEPHRECTOMY PLUS MEDROXYPROGESTERONE ACETATE FOR METASTATIC RENAL CELL CARCINOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7956

OBJECTIVES:

I. Determine the response rate and survival patterns in patients with disseminated renal cell carcinoma treated with postinfarction nephrectomy.

II. Determine the response rate and survival patterns of patients with disseminated renal cell carcinoma who relapse or do not respond to postinfarction nephrectomy when treated with medroxyprogesterone acetate (MPA).

PROTOCOL ENTRY CRITERIA: Patients with measurable, disseminated renal cell carcinoma who have not undergone nephrectomy and in whom metastatic disease is not amenable to surgery. Patients must have a minimum life expectancy of 3 months and a SWOG performance status of 3 or less. Patients must have adequate contralateral kidney function and negative urine culture. Patients must have had no prior MPA, chemotherapy, or radiotherapy of the primary.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with progressive disease after Regimen A to Regimen B.

Regimen A: Surgery. Renal infarction plus nephrectomy.

Regimen B: Single-agent Hormone Therapy. Medroxyprogesterone acetate, MPA, NSC-26386.

STRATIFICATION: Participating institutions; performance status: 0-1 vs. 2-3.

SPECIAL STUDY PARAMETERS: IVP, bone and liver scans, renal and hepatic function.

END POINTS: Objective tumor response, response/remission rate, survival rate, relapse rate.

CURRENT STATUS: At least 25 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Renal infarction on day 1. Radical nephrectomy on day 5, 6 or 7. Patients with progressive disease enter Regimen B.

Regimen B: MPA - 800 mg im q 7 days. Remove patients from study if disease progresses after 6 courses.

Follow all patients for survival.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: MPA - 100 mg vials.

DATE SUMMARIZED: 02/80

3.0030 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR METASTATIC RENAL CELL CARCINOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7959

OBJECTIVES:

I. Determine the response rate and remission duration with methyl-GAG (MeGAG) for metastatic renal carcinoma.

II. Define the qualitative and quantitative toxicity of MeGAG.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven, incurable, metastatic renal cell carcinoma. Patients must have a minimum life expectancy of 6 weeks and a SWOG performance status of 2 or better. Patients must have adequate hematologic, hepatic and renal function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, duration of response and survival, toxicity/morbidity of treatment.

CURRENT STATUS: At least 25 patients to be entered in 6 months.

DOSAGE SCHEDULE:

MeGAG - 600 mg/sqm iv weekly. Evaluate for response after 3 courses. Remove patients with progressive disease or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeGAG - 1 g vials.

DATE SUMMARIZED: 02/80

3.0031 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE (DHAD) FOR ADVANCED RENAL CELL CARCINOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-8011

OBJECTIVES:

I. Determine the response rate and duration of response in patients with advanced renal cell carcinoma treated with dihydroxyanthracenedione used in a single dose every-three-week schedule.

II. Define the qualitative and quantitative toxicities of dihydroxyanthracenedione administered in a Phase II study.

PROTOCOL ENTRY CRITERIA: Patients of all ages with advanced renal cell carcinoma with clearly measurable disease who are not eligible for higher priority SWOG protocols. Patients must have a life expectancy of at least 6 weeks, and a performance status of 2 (Karnofsky 50-60) or better. The pretreatment WBC must be 3500/cumm or greater; platelet count must be 125,000/cumm or greater; and serum creatinine and bilirubin must be 2.0 mg percent or less. No other chemotherapeutic agents or radiation therapy may be given comcomitantly and patients must have recovered from the acute toxicities of any prior therapy; the nadirs of leukopenia and thrombocytopenia must have been surpassed with evidence of hematologic recovery.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Participating institutions; prior chemotherapy: yes vs. no.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; tumor measurements; chest x-ray; EKG.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, recurrence rate.

CURRENT STATUS: 14 patients will be entered.

DOSAGE SCHEDULE:

DHAD - 12 mg/sqm through a free-running iv over 30 minutes q 3 weeks, provided patient has recovered from previous drug-induced toxicity. Patients who show disease progression or unacceptable stable disease after 2 courses go off study. Those who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 5 mg ampules.

DATE SUMMARIZED: 10/80

3.0032 TAMOXIFEN AND MEDROXYPROGESTERONE ACETATE FOR DISSEMINATED RENAL CELL CARCINOMA

Aisner, J., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7817

OBJECTIVES:

I. Determine the response rate and survival of patients with disseminated renal cell carcinoma treated with tamoxifen and medroxyprogesterone acetate.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven disseminated renal cell carcinoma who have not received prior hormonal agents. Patients must have measurable disease and an expected survival of at least 8 weeks. Prior chemotherapy must have been terminated at least 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Hormone Therapy. Tamoxifen, TMX, NSC-180973; Medroxyprogesterone acetate, MPA, NSC-26386.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements, performance status, hemogram, kidney and liver function tests, serum calcium if abnormal initially, appropriate scans and x-rays for tumor measurements.

END POINTS: Response/remission rate, duration of response, survival, objective tumor response.

CURRENT STATUS: An estimated 14-19 patients will be accrued in 18 months.

DOSAGE SCHEDULE:

TMX - 30 mg/day po in 3 divided doses for at least 8 weeks; MPA - 1000 mg/week im. Discontinue therapy after 8 weeks in case of progressive disease; continue patients with objective response until there is evidence of progression.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

3.0033 PHASE II EVALUATION OF METHYL-GAG IN PATIENTS WITH DISSEMINATED CARCINOMA OF THE KIDNEY

Van Echo, D. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7921

OBJECTIVES:

I. Determine the therapeutic efficacy of methyl-GAG in the treatment of patients with metastatic renal cell carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven disseminated renal cell carcinoma who have measurable disease not amenable to surgery, radiotherapy, or a higher priority protocol. The expected survival must be greater than 8 weeks. There may have been no prior treatment with methyl-GAG and no chemotherapy or radiotherapy within 4 weeks of entry on study. There may be no history of a previous second primary malignant neoplasm other than cured basal cell carcinoma of the skin or surgically removed in situ carcinoma of the cervix.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-12, electrolytes, serum creatinine, chest x-ray with optional tomography, metastatic bone survey in suspicious cases, IVP as indicated, liver/spleen scan, bone scan and brain CAT scan if indicated, EKG, bone marrow biopsy if there is evidence of myelosuppression.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Initially, 10-20 patients will be entered during 12 months to determine whether or not there is a response to treatment. If a clinical response is demonstrated, an additional 10-20 patients will be entered during the next 12 months.

DOSAGE SCHEDULE:

MeGAG - 500 mg/sqm iv over 60 minutes. Repeat weekly. At 4-week intervals and in the absence of hematologic toxicity, increase dose by 100 mg/sqm. After 12 doses, remove those with progressive disease and life-threatening toxicities from study; continue responders until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeGAG - 1 g vials.

DATE SUMMARIZED: 12/80

3.0034 PHASE II CHEMOTHERAPY WITH CL 216,942 ON A SINGLE-DOSE SCHEDULE FOR ADVANCED RENAL CELL CARCINOMA

Van Echo, D. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-8031

OBJECTIVES:

I. Determine the therapeutic efficacy of the iv anthracenedicarboxaldehyde hydrazone CL 216,942 administered every 3-4 weeks in patients with advanced renal cell carcinoma.

II. Determine the toxicities and other adverse occurrences following the iv administration of CL 216,942.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented, advanced renal cell carcinoma who have clearly measurable disease and who have recovered from all prior therapy. The life expectancy must be at least 6 weeks and the performance status no worse than 2 (50-60 on the Karnofsky scale). There must be adequate bone marrow, renal, and hepatic function, and there may be no gross alterations in biochemical parameters. Cardiac status must be stable.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. 9,10-Anthracenedicarboxaldehyde bis [(4,5-dihydro-1H-imidazol-2-yl)hydrazone] dihydrochloride, CL 216, 942.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, chest x-ray, EKG, appropriate x-rays and scans.

END POINTS: Survival time, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 14-25 patients will be entered.

DOSAGE SCHEDULE:

CL 216,942 - 260 mg/sqm iv over at least 1 hour repeated q 3 weeks; escalate to 280 mg/sqm in the absence of side effects.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 80, 200, and 450 mg vials.

DATE SUMMARIZED: 01/81

3.0035 PERCUTANEOUS TRANSFEMORAL RENAL ARTERY OCCLUSION, NEPHRECTOMY AND HORMONAL THERAPY WITH MEDROXYPROGESTERONE ACETATE FOR RENAL CARCINOMA

Johnson, D. E., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-162

OBJECTIVES:

I. Determine the efficacy of combination percutaneous selective renal artery occlusion, nephrectomy, and MPA therapy in patients with metastatic renal carcinoma.

II. Record possible immunological changes occurring after renal tumor infarction.

PROTOCOL ENTRY CRITERIA: Patients with histologically or angiographically confirmed carcinoma of the renal parenchyma with metastases. Patients must have a measurable lesion in the lung or superficial soft tissue.

PROTOCOL OUTLINE: Nonrandomized study.

Percutaneous Transfemoral Selective Renal Infarction plus Transabdominal Nephrectomy plus Single-agent Hormone Therapy. Medroxyprogesterone acetate, MPA, NSC-26386.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Toxicity/morbidity of treatment, response/remission rate.

CURRENT STATUS: 15 patients will be entered per year.

DOSAGE SCHEDULE:

Percutaneous Transfemoral Selective Renal Infarction is followed in 5-7 days by Transabdominal Nephrectomy. Following Nephrectomy begin MPA - 400 mg im twice a week for a minimum of 12 weeks until progression.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

3.0036 ORAL ESTRACYT FOR METASTATIC RENAL CARCINOMA

Johnson, D. E., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-316; MDA-U32/U24

OBJECTIVES:

I. Determine the efficacy of oral estracyt in patients with metastatic renal carcinoma.

II. Monitor the qualitative and quantitative toxicity of this therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed carcinoma of the renal parenchyma or definite angiographic evidence of the disease with metastases and some measurable lesion, exclusive of bone. Patients must have an expected survival of at least 90 days, adequate hematologic function and no other neoplasm.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Hormonal Therapy. Estracyt, NSC-89199.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, response/remission rate.

CURRENT STATUS: 15 patients will be entered within 18 months.

DOSAGE SCHEDULE:

Estracyt - 600 mg/sqm/day given in 3 divided doses po for 12 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Estracyt - not given.

DATE SUMMARIZED: 06/79

3.0037 PHASE II-III CHEMOTHERAPY WITH CONTINUOUS 5-DAY VINDESINE INFUSION FOR METASTATIC RENAL CARCINOMA

Bodey, G. P., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-327; MDA-DT-7913

OBJECTIVES:

I. Determine the therapeutic efficacy in terms of response rate and survival of continuous 5-day infusion of vindesine for metastatic renal carcinoma.

II. Determine the toxicity of this therapy.

PROTOCOL ENTRY CRITERIA: Patients with measurable, metastatic or inoperable renal cancer who have had no prior exposure to vinca alkaloids. Patients must have a life expectancy of at least 8 weeks, be off all prior chemotherapy for at least 3 weeks and fully recovered from its toxicity, and be off hormonal therapy for at least 6 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: A minimum of 25 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 1.2 mg/sqm for good risk patients, 1.0 mg/sqm for poor risk patients (with inadequate bone marrow reserve and abnormal liver function) iv 24 hr infusion for 5 days q 3 weeks. Increase dosage to 1.4 mg/sqm if granulocytes are above 2000 and platelets above 100, 000, and decrease dosage to 1.0 mg/sqm if granulocytes are below 1000 and platelets below 50,000.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

3.0038 IMMUNOTHERAPY WITH BCG AND RENAL CANCER CELLS FOR STAGE II-IV RENAL CANCER

Livingston, P. O., Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York, 10021, United States of America

PROTOCOL NUMBER(S) MSKCC-796

OBJECTIVES:

I. Determine whether treatment with cultured renal cancer cells and BCG results in changes in the titer of antibodies against autologous renal cancer cells.

PROTOCOL ENTRY CRITERIA: Patients with Stage II-IV renal cancer, provided their autologous tumor cells can be established in continuous tissue culture as target cells for serological tests and they are able to return for the necessary followup studies.

PROTOCOL OUTLINE: Nonrandomized study.

Surgery plus Immunotherapy. BCG-unspecified plus irradiated cultured allogenic renal cancer cells.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Serial pre- and postvaccine sera are tested on cultured autologous renal cancer cells. Specificity of observed reactions is studied with extensive absorption analysis.

END POINTS: Objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 20 patients will be entered in 2 years.

DOSAGE SCHEDULE:

BCG - 2-6 x 10 to the seventh viable units by multiple tine technique to 2 quadrants, rotating, beginning 2 weeks after surgery; dose may be adjusted depending upon observed skin reaction. Allogenic renal cancer cells - 2 x 10 to the seventh viable cultured cells, irradiated with 10,000 rads, id q 21 days into 2 sites innoculated with BCG earlier, beginning 3 weeks after surgery. Autologous renal cancer cells may be prepared and administered as described for allogenic renal cancer cells. Evidence of progressive renal cancer after 3 months terminates treatment; otherwise, treatment will continue for one year. In the absence of progressive disease after 1 year, an additional year at double intervals may be given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

3.0039 CROSS-OVER IMMUNOTHERAPY WITH POLYMERIZED TUMOR ANTIGEN-ADJUVANT AND HORMONAL THERAPY WITH PROGESTERONE FOR RENAL CANCER

Neidhart, J. A., The Ohio State University Hospitals, 410 West Tenth Avenue, Room N-1022, Columbus, Ohio, 43210, United States of America

PROTOCOL NUMBER(S) OH-REN-OSU-7902

OBJECTIVES:

I. Determine the efficacy of tumor antigen preparations modified by aggregation and admixed with tuberculin in the therapy of advanced renal carcinoma and in preventing recurrence of renal cancer in high-risk patients (adjuvant).

PROTOCOL ENTRY CRITERIA: Patients with previously untreated advanced renal cancer or surgically resected renal cancer with no residual disease but with high-risk recurrence.

PROTOCOL OUTLINE: Randomized study. Group I (previously untreated) patients are randomized to Arm I or II; Group II (surgically resected) patients enter Arm II or III.

Arm I: Immunotherapy. Polymerized tumor antigen-adjuvant, PTA/Ad.

Arm II: Hormone Therapy. Progesterone, NSC-9704.

Arm III: No treatment. Placebo.

Arm I patients who show progression cross over to Arm II; Arm II patients showing progression cross over to Arm I. Arm III patients showing progression cross over to Arm I.

STRATIFICATION BY: Disease sites.

SPECIAL STUDY PARAMETERS: Immunologic evaluation with skin tests, in-vitro assay.

END POINTS: Response of measurable disease, disease recurrence.

CURRENT STATUS: 15 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: PTA/Ad - 250 micrograms sc q 2 weeks for 4 months.

Arm II: Progesterone - 1000 mg im weekly for 4 weeks, then 400 mg weekly for 8 weeks, thereafter 400 mg monthly if no progression.

Arm III: Placebo.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 00150280

3.0040 ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE FOR STAGE II AND III RENAL CELL CARCINOMA

Harvey, H. A., (717-534-8677) The Milton S. Hershey Medical Center, The Pennsylvania State University, Dept. of Medicine/Div. of Oncology, Hershey, Pennsylvania, 17033, United States of America

PROTOCOL NUMBER(S) PA-MSHMC-REN-1; JRD-12564/015C

OBJECTIVES:

I. Assess the effectiveness of adjuvant immunotherapy with levamisole for carcinoma of the kidney.

II. Evaluate the effect of two years of treatment with levamisole.

PROTOCOL ENTRY CRITERIA: Patients at least 18 years of age with Stage II or III adenocarcinoma of the kidney; they shall have undergone radical nephrectomy.

PROTOCOL OUTLINE: Randomized, double-blind study.

Arm I: Immunotherapy. Levamisole, LEV, NSC-177023.

Arm II: Placebo.

STRATIFICATION BY: Disease stage: II vs. III.

SPECIAL STUDY PARAMETERS: Skin tests for delayed hypersensitivity.

END POINTS: Relapse/recurrence rate, disease-free interval, rate and duration of survival, toxicity.

CURRENT STATUS: 19 patients have been accrued as of February 1980.

DOSAGE SCHEDULE:

Arm I: LEV - 2.5 mg/kg po on 2 consecutive days each week for 24 months.

Arm II: Placebo - tablet identical to LEV, on same schedule.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: LEV - 50 mg film-coated tablets; placebo tablets.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

3.0041 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED RENAL CELL CARCINOMA

Child, J. A., European Org. for Research on Treatment of Cancer, Genitourinary Tract Cancer Cooperative Group, The General Infirmary at Leeds, Great George Street, Leeds LS1 3EX, United Kingdom

PROTOCOL NUMBER(S) EORTC-30801

OBJECTIVES:

I. Determine the objective tumor response rate and response duration produced by methyl-GAG in patients with measurable metastases from renal cell carcinoma.

II. Define the morbidity of the treatment.

PROTOCOL ENTRY CRITERIA: Patients with nonoperable metastases of histologically or cytologically proven renal cell carcinoma and measurable or evaluable lesions. Patients must be under 75 years of age, have an acceptable performance status (Karnofsky index of greater than 60 or ECOG I and II) and adequate hematologic and renal function. Patients must not have a second tumor (except basal cell skin cancer) or brain metastases.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements: x-ray, isotopic, or CT scans or ultrasonic echography; hematologic, renal, and hepatic function tests.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment, disease-free interval.

CURRENT STATUS: 29 patients will be entered.

DOSAGE SCHEDULE:

MeGAG - 500 mg/sqm iv over 30 minutes on day 1, repeated weekly. Patients with progressive disease after 7 courses and those with persisting toxicity will be taken off study. Patients showing regression or stabilization of disease will continue treatment until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

3C. PROSTATE

3.0042 PILOT IMMUNOTHERAPY WITH LEVAMISOLE ADJUVANT TO DIETHYLSTILBESTROL THERAPY FOR STAGE D ADENOCARCINOMA OF THE PROSTATE

Carbone, P., (608-263-6650) Eastern Cooperative Oncology
Group, 905 University Ave., Suite 415, Madison, Wisconsin,
53715, United States of America
PROTOCOL NUMBER(S) EST-PB-879

OBJECTIVES:

I. Determine whether the addition of levamisole (LEV) to estrogen therapy causes significant morbidity or mortality.

II. Determine whether LEV in addition to conventional diethylstilbesterol (DES) therapy will counteract the immunologic deficits caused by DES alone.

III. Gain information to aid in the design of future randomized ECOG trials for Stage D prostatic carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with measurable histologically confirmed Stage D adenocarcinoma of the prostate. Patients must have a minimum life expectancy of 3 months and no prior chemotherapy including LEV or estrogens, and an adequate cardiac status.

PROTOCOL OUTLINE: Nonrandomized study.

Hormone Therapy plus Immunotherapy. Diethylstilbesterol, DES, NSC-3070; plus Levamisole, LEV, NSC-177023.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: IVP, immune status including PHA and PWM blastogenesis and LAI, liver scan.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response, survival time.

CURRENT STATUS: 25 to 30 patients will be entered in 1 year.

DOSAGE SCHEDULE:

DES - 3 mg/day po for 2 months. Then begin immunotherapy while continuing hormone therapy. LEV - 2.5 mg/kg/day given po in 2 divided doses on 3 days q 2 weeks. Continue both therapies until disease progresses or severe toxicity ensues. Patients may undergo orchiectomy, and may be given supportive therapy with compazine.

Dosage modifications for toxicity are given.

DOSAGE FORMS: LEV - 50 mg tablets; DES - 1 mg tablets.

DATE SUMMARIZED: 11/79

3.0043 PHASE II PILOT CHEMOTHERAPY WITH CACP FOR ADVANCED (STAGE D) PROSTATIC CARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology
Group, 905 University Ave., Suite 415, Madison, Wisconsin,
53715, United States of America
PROTOCOL NUMBER(S) EST-PD-879

OBJECTIVES:

I. Determine a tolerable dose schedule of cis-platinum administration in an outpatient setting for patients with advanced prostatic carcinoma.

II. Make a preliminary estimate of the efficacy of cis-platinum in advanced prostatic carcinoma in an effort to determine whether this regimen should be included in Phase III studies.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed adenocarcinoma of the prostate not amenable to surgery or radiation therapy. Patients may be previously untreated or may have relapsed after or failed to respond to ablative or additive hormonal therapy. Patients must have either measurable disease or an elevated acid phosphatase. The performance status must be 0-3, hematologic and renal parameters must be adequate, and the patient may not be older than 75 years.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, renal function tests, measurement of lesion, chest x-ray, serum acid phosphatase, ultrasound/transrectal, CAT.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: A maximum of 20 patients will be entered.

DOSAGE SCHEDULE:

CACP - 50 mg/sqm iv q 3 weeks with concomitant mannitol-furosemide diuresis. Therapy will continue until there is evidence of disease progression according to ECOG criteria or until prohibitive toxicity develops.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 07/80

3.0044 PHASE III ADR VS ADR/CIS-PLATINUM CHEMOTHERAPY FOR ENDOCRINE UNRESPONSIVE METASTATIC ADENOCARCINOMA OF THE PROSTATE

Carter, S. K., (415-497-7512) Northern California Oncology
Group, 1801 Page Mill Rd., Bldg. B Suite 200, Palo Alto,
California, 94304, United States of America
PROTOCOL NUMBER(S) NCOG-4P81

OBJECTIVES:

I. Compare the effects of chemotherapy with adriamycin (ADR) alone to the effects of ADR/cis-platinum in patients with Stage D endocrine-unresponsive cancer of the prostate.

PROTOCOL ENTRY CRITERIA: Patients not over 70 years of age with histologically confirmed carcinoma, metastatic adenocarcinoma of the prostate, Stage D, not amenable to curative surgery or radiotherapy and relapsed or failed to respond to hormone therapy or orchiectomy (Revision June 1979). Patients must have measurable tumor and/or elevated acid phosphatase, adequate hepatic, renal and bone marrow function and a Karnofsky performance status not below 70%. They must not have had prior chemotherapy, must have stopped all hormonal therapy, and must not have had radiotherapy to the heart of more than 1000 rad.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: 2-Drug Combination Chemotherapy. ADR, plus cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions; measurable tumor vs. no measurable tumor; prior radiotherapy: none or limited vs. extensive; serum acid phosphatase: normal vs. elevated; primary tumor histology: well vs. moderately vs. poorly differentiated (Revision, June 1979).

SPECIAL STUDY PARAMETERS: Liver scan, ultrasound or CT scan; lymphangiogram; IVP; bone and abdominal (optional) CT scan; LH; audiogram; FSH; sexual function.

END POINTS: Disease-free interval, time to regression, time to subjective improvement, time to progression, pattern of relapse, objective tumor response, response rate, survival time.

CURRENT STATUS: 100 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Maintain all patients without orchiectomy on 1 mg diethylstilbestrol, DES, NSC-3070, for the duration of Chemotherapy.

Arm I: ADR - 60 mg/sqm (40 mg/sqm for patients with extensive Radiotherapy) iv given in 30 to 60 min q 21 days. Upon disease progression, cross over patients to CACP, as in Arm II.

Arm II: ADR, as in Arm I, plus CACP - 80 mg/sqm (60 mg/sqm for patients with extensive Radiotherapy) iv 24 hours infusion with adequate hydration.

Discontinue ADR in Arms I and II when the maximum cumulative dose of 450 mg/sqm has been given.

Discontinue therapy upon disease progression. Follow all patients for at least 5 years and for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules; CACP - 10 mg vials.

DATE SUMMARIZED: 08/79

3.0045 PHASE III THERAPY WITH DES VS DES/ADR FOR METASTATIC ADENOCARCINOMA OF THE PROSTATE

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PROTOCOL NUMBER(S) NCOG-4P82

OBJECTIVES:

I. Compare the effects of hormone therapy with diethylstilbestrol (DES) alone to the effects of DES and adriamycin (ADR) in patients with Stage D (at presentation or after failure of local therapy) cancer of the prostate.

PROTOCOL ENTRY CRITERIA: Patients not over 70 years of age with histologically confirmed metastatic adenocarcinoma of the prostate Stage D not amenable to curative surgery or radiotherapy. Patients must have measurable tumor and/or elevated acid phosphatase, adequate hepatic, renal and bone marrow function, and a Karnofsky performance status not below 70%. They must not have had prior chemotherapy or radiation therapy to the heart of more than 1000 rad.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Hormone Therapy. Diethylstibestrol, DES, NSC-3070.

Arm II: Single-agent Hormone Therapy plus Single-agent Chemotherapy. DES; plus Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions; measurable tumor vs. no measurable tumor; prior radiotherapy: none or limited vs. extensive; serum acid phosphatase: normal vs. elevated; Stage D disease status at presentation vs. following failure of primary local therapy.

SPECIAL STUDY PARAMETERS: Liver and bone scan, ultrasound or CT scan, lymphangiogram, abdominal (optional) CT scan, LH, audiogram, FSH, sexual function, IVP.

END POINTS: Disease-free interval, time to regression, time to subjective improvement, time to progression, pattern of relapse, objective tumor response, response rate, survival time.

CURRENT STATUS: 100 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: DES - 1 mg/day po until disease progression. At failure patients may be entered to protocol NCOG-4P81.

Arm II: DES, as in Arm I; plus ADR - 60 mg/sqm (40 mg/sqm for patients with extensive radiotherapy) iv q 21 days. Discontinue ADR when a cumulative dose of 450 mg/sqm has been given. Discontinue ADR and DES on disease progression.

Follow up all patients for at least 5 years and for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg capsules; DES - 0.1 to 5 mg tablets.

DATE SUMMARIZED: 05/79

3.0046 RADIOTHERAPY FOLLOWED BY ESTRACYT OR CTX FOR PROSTATIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) NPCP-1000

OBJECTIVES:

I. Evaluate the efficacy of adjuvant chemotherapy, estracyt or cyclophosphamide (CTX), in patients who have had definitive radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven Stage B2, C or D1 prostatic carcinoma with no evidence of metastases to bones or soft tissue above the pelvis. Patients must have had a retroperitoneal node dissection but no other prior surgery or treatment for this condition. Patients must have adequate blood counts.

PROTOCOL OUTLINE: Assign all patients to Regimen A, then randomize to Arms I, II, and III.

Regimen A: Definitive Radiotherapy.

Arm I: Single-agent Hormone Therapy. Estracyt, NSC-89199.

–Arm II: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm III: No treatment.

STRATIFICATION BY: Participating institutions, nodal status.

SPECIAL STUDY PARAMETERS: IVP, bone scan, acid and alkaline phosphatase, renal and hepatic function tests.

END POINTS: Response/remission rate, disease-free interval, survival rate, time to appearance of metastases, survival time.

CURRENT STATUS: 249 patients will be entered in 2-3 years.

DOSAGE SCHEDULE:

Arm I: 6600 to 7020 rads in 6.5 to 8 weeks to prostate and immediate periprostatic tissues of patients with histologically negative lymph nodes, 6640 to 7020 rads in 7 to 8 weeks to prostate and regional pelvic nodes of patients with histologically positive nodes. Begin all Chemotherapy within 30 days of the completion of Radiotherapy.

Arm II: Estracyt - 600 mg/sqm/day po in 3 divided doses for 1 year.

Arm III: CTX - 1.0 gm/sqm iv single dose q 3 weeks for 1 year.

Arm IV: No treatment.

After 1 year of Chemotherapy, evaluate the feasibility of continuing treatment. At progression of disease, patients are randomized to appropriate NPCP protocols. Follow all patients for life.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; Estracyt - not given.

DATE SUMMARIZED: 09/78

3.0047 COMPARISON OF ESTRACYT, CACP, AND MTX AS SINGLE AGENTS IN HORMONE-REFRACTORY PATIENTS WITH ADVANCED PROSTATIC CANCER

Murphy, G. P., (716-845-5770) National Prostatic Cancer Project, c/o Roswell Park Memorial Instit, Buffalo, New York, 14263, United States of America
PROTOCOL NUMBER(S) NPCP-1100

OBJECTIVES:

I. Compare the activities of methotrexate, estracyt, and cis-platinum as single agents in the treatment of patients with metastatic prostatic carcinoma who have failed on endocrine therapies and who have not received prior radiotherapy.

II. Study the sequential effects of these agents by a suitable crossover design at progression.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented metastatic prostatic carcinoma who have not received previous radiotherapy and who have failed on endocrine therapies, including orchiectomy. At least 4 to 6 weeks must have elapsed since orchiectomy. The expected survival must be at least 90 days; kidney, liver, and bone marrow function must be adequate. No hormonal therapy shall have been administered within the 14 days prior to entry. Patients may not have received treatment with any of the study drugs prior to entry. There may be no history of another neoplasm, aside from nonmelanomatous skin cancer.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I, II, or III.

Arm I: Single-agent Chemotherapy. Methotrexate, MTX, NSC-740.

Arm II: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm III: Single-agent Chemotherapy. Estracyt, ESC, NSC-89199.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, kidney and liver function tests, acid and alkaline phosphatase, chest x-ray, skeletal survey and/or bone scan, IVP.

END POINTS: Response/remission rate, duration of response, duration of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 180 patients will be entered.

DOSAGE SCHEDULE:

Arm I: MTX - 40 mg/sqm iv on day 1, 60 mg/sqm iv on day 8 and q 7 days thereafter.

Arm II: CACP - 60 mg/sqm iv over 15 minutes with adequate prehydration and post-treatment mannitol diuresis.

Arm III: ESC - 600 mg/sqm/day po in 3 divided doses.

All patients will be treated for 12 weeks. If remission or clinical benefit results, treatment may be continued indefinitely. Patients on MTX or CACP who progress after 12 weeks will be crossed over to ESC. Patients on ESC who progress after 12 weeks will be randomized to receive either MTX or CACP.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 50 mg vials; CACP - 10 mg ampules; ESC - 140 mg tablets.

DATE SUMMARIZED: 01/81

3.0048 COMPARISON OF CACP VS ESTRACYT VS CACP/ESTRACYT IN STAGE D PROSTATIC CARCINOMA FOLLOWING EXTENSIVE RADIOTHERAPY

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United States of America
PROTOCOL NUMBER(S) NPCP-1200

OBJECTIVES:

I. Compare cis-platinum and estracyt as single agents and combined for their therapeutic effectiveness in treating patients with Stage D prostatic carcinoma who are refractory to hormone therapy and who have received radiotherapy of at least 2000 rads to the pelvis and/or the lumbosacral area.

II. Study the sequential effects of these single agents by a suitable crossover design at progression.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage D prostatic carcinoma who have failed on endocrine therapy, including orchiectomy, and who have received at least 2000 rads to the pelvis and/or lumbosacral area. Patients must have an expected survival of at least 90 days and must have adequate renal, hepatic, and bone marrow function. Patients must have recovered from the effects of major surgery and be free of significant infection, and there may have been no hormonal therapy within the 14 days prior to entry. Patients may not have been previously treated with either of the study drugs. There may be no history of another neoplasm, aside from nonmelanomatous skin cancer.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I, II, or III.

Arm I: Single-agent Hormone Therapy. Estracyt, ESC, NSC-89199.

Arm II: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm III: Single-agent Chemotherapy plus Single-agent Hormone Therapy. CACP; ESC.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, acid and alkaline phosphatase, chest x-ray and skeletal survey and/or bone scan, IVP.

END POINTS: Response/remission rate, duration of response, duration of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 180 patients will be entered.

DOSAGE SCHEDULE:

Arm I: ESC - 600 mg/sqm/day po in 3 divided doses.

Arm II: CACP - 60 mg/sqm iv over 15 minutes on days 1 and 21, thereafter q month. Prehydrate and follow treatment with mannitol diuresis.

Arm III: ESC - as in Arm I; CACP - as in Arm II.

Treat all patients for at least 12 weeks. If remission, clinical benefit, or disease stability results, continue treatment indefinitely. Patients treated with CACP or ESC who progress after 12 weeks should be crossed over.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg ampules; ESC - 140 mg tablets.

DATE SUMMARIZED: 12/80

3.0049 DES OR ORCHIECTOMY VS CTX/5-FU PLUS DES OR ORCHIECTOMY VS ESTRACYT FOR STAGE D PROSTATE CANCER WITHOUT PRIOR HORMONAL THERAPY OR CHEMOTHERAPY

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PROTOCOL NUMBER(S) NPCP-1300

OBJECTIVES:

I. Compare diethylstilbestrol (DES) or orchiectomy vs. cyclophosphamide (CTX)/5-fluorouracil (5-FU) plus DES or orchiectomy vs. estracyt in the treatment of newly diagnosed patients with clinical Stage D carcinoma of the prostate who have not previously been treated with chemotherapy or endocrine therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed cancer of the prostate diagnosed within 30 days of randomization who have bone or demonstrable soft tissue metastases that are Stage D2. The expected survival must be at least 90 days, and bone marrow function must be adequate. Patients must have recovered from the effects of major surgery and be free from significant infection. There may have been no prior chemotherapy or hormonal therapy, nor may there be present another malignancy (with the exception of nonmelanomatous skin tumors).

PROTOCOL OUTLINE: Randomized study.

Arm I: Hormone Therapy. Diethylstilbestrol, DES, NSC-3070; or Orchiectomy.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893; plus DES or Orchiectomy.

Arm III: Single-agent Chemotherapy. Estracyt, ESC, NSC-89199.

STRATIFICATION BY: Participating institutions, pelvic and/or lumbosacral radiotherapy (more vs. less than 2000 rads), site of metastases (soft tissue alone or soft tissue plus bone).

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, acid and alkaline phosphatase, chest x-ray and skeletal survey, bone scan, IVP.

END POINTS: Response/remission rate, duration of response, duration of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 333 patients will be entered.

DOSAGE SCHEDULE:

Arm I: DES - 3 mg/day po in 3 divided doses; or orchiectomy.

Arm II: CTX - 650 mg/sqm iv push q 3 weeks; 5-FU - 350 mg/sqm/week iv push; DES - 3 mg/day po in 3 divided doses, or orchiectomy.

Arm III: ESC - 600 mg/sqm/day po in 3 divided doses.

Treatment is to be indefinite as long as the patient is stable. Upon progression of disease, patients in Arms I and II will be crossed over to Arm III and those in Arm III will be crossed over to Arm II. Following progression after crossover, treatment will consist of Prednisone and orchiectomy, if not already performed.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DES - 1 mg tablets; CTX - 100, 200, and 500 mg vials; 5-FU - 500 mg vials; ESC - 140 mg tablets.

DATE SUMMARIZED: 01/81

3.0050 HORMONE THERAPY WITH DES ALONE OR COMBINED WITH CTX OR ESTRACYT FOR PROSTATIC CARCINOMA STAGE D

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14263, United States of America
PROTOCOL NUMBER(S) NPCP-600

OBJECTIVES:

I. Determine the efficacy of the addition of therapy with estracyt or cyclophosphamide (CTX) to estrogen therapy with diethylstilbestrol (DES) as a means of controlling Stage D prostatic carcinoma. The study will determine the success of therapy in part by the prevention of recurrence, duration of stability, and/or absence of progression

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage D metastatic carcinoma of the prostate who have been unsuccessfully treated by orchiectomy, or by estrogen therapy (3 to 5 mg daily) for at least 12 weeks prior to entry into the study. Therapy must not have included antiandrogens. Patients must have adequate blood counts and an expected survival time of at least 120 days. Patients must not have had prior therapy with study agents.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Hormone Therapy. Diethylstilbestrol, DES, NSC-3070.

Arm II: Single-agent Hormone Therapy plus Single-agent Chemotherapy. DES; Cyclophosphamide, CTX, NSC-26271.

Arm III: 2-Drug Combination Hormone Therapy. DES; Estracyt, NSC-89199.

STRATIFICATION BY: Participating institutions; orchiectomy; prior extensive pelvic irradiation (over 2000 rads).

SPECIAL STUDY PARAMETERS: Renal and hepatic function tests, bone scan, IVP.

END POINTS: Response/remission rate, disease progression, duration of response, toxicity/morbidity of treatment, survival rate, objective tumor response.

CURRENT STATUS: 294 patients will be entered.

DOSAGE SCHEDULE:

Arm I: DES - 3 mg/day po in three divided doses.

Arm II: DES as in Arm I; plus CTX - 1 gm/sqm iv single dose q 3 weeks.

Arm III: DES as in Arm I; Estracyt - 600 mg/sqm/day po in 3 divided doses.

Continue therapy for all patients until progression of disease is evident, then reassign to appropriate NPCP protocols.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; DES - 1 mg tablets; Estracyt - not given.

DATE SUMMARIZED: 09/78

3.0051 HORMONE THERAPY WITH ESTRACYT VS CHEMOTHERAPY WITH CTX AFTER PROSTATECTOMY FOR PROSTATIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) NPCP-900

OBJECTIVES:

I. Evaluate the efficacy of adjuvant chemotherapy, estracyt or cyclophosphamide (CTX) in patients who have had prior total prostatectomy (or cryosurgery) plus lymph node dissection.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven Stage B2, C or D1 prostatic carcinoma without distant metastases. Patients must have had a total prostatectomy or cryosurgery, plus lymph node dissection but no other prior therapy. Patients must have adequate blood counts.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Hormone Therapy. Estracyt, NSC-89199.

Arm II: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm III: No treatment.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tests of renal and hepatic function, acid and alkaline phosphatase, bone scan, IVP.

END POINTS: Response/remission rate, disease-free interval, survival rate, duration of survival, time to appearance of metastases.

CURRENT STATUS: 249 patients will be entered in 3 years.

DOSAGE SCHEDULE: Enter patients within 6 weeks of surgery.

Arm I: Estracyt - 600 mg/sqm/day po in 3 divided doses for 3 years.

Arm II: CTX - 1.0 gm/sqm iv q 3 weeks for 3 years.

Arm III: No treatment.

At progression of disease, randomize patients to appropriate NPCP protocols.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; Estracyt not given.

DATE SUMMARIZED: 09/78

3.0052 RADIOTHERAPY AND HORMONAL THERAPY WITH STILPHOSTROL FOR STAGE C ADENOCARCINOMA OF THE PROSTATE

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PROTOCOL NUMBER(S) RTOG-7506

OBJECTIVES:

I. Determine the value of pelvic vs. pelvic plus para-aortic nodal irradiation (when common iliac and para-aortic nodes are negative or unevaluated), and the value of pelvic plus para-aortic nodal irradiation vs. pelvic, para-aortic, mediastinal and supraclavicular irradiation (when common iliac and/or para-aortic nodes are positive) in locally advanced prostate cancer as measured by relapse-free survival and total survival.

II. Determine whether radiation therapy is superior to hormonal therapy as measured by the relapse-free survival, total survival and complications and reactions.

III. Determine the value of the rate of tumor clearance and post-irradiation biopsy of the prostate cancer bed in predicting long-term local control (cure).

PROTOCOL ENTRY CRITERIA: Patients with Stage C adenocarcinoma of the prostate who have not had curative surgery and who have lymphangiogram or laparotomy evidence of lymph node involvement. (Note: Although lymphangiogram and laparotomy are used to determine treatment group in this protocol, the staging is clinical, and is not changed by lymphangiogram or laparotomy findings.) Protocol revised to allow Stage B patients with positive pelvic nodes 11/77.)

PROTOCOL OUTLINE: Randomized study. Enter patients with positive pelvic nodes and negative common iliac and para-aortic lymph nodes or with unknown nodal status or with no positive nodes.

Arm I: Single-agent Hormone Therapy. Stilphostrol, NSC-10481; or Diethylstilbestrol, DES, NSC-3070. (Arm terminated by 6/77 revision.)

Arm II: Radiotherapy. Irradiation of pelvic nodes.

Arm III: Radiotherapy. Irradiation of pelvic and para-aortic nodes.

Enter patients with positive common iliac and/or para-aortic lymph nodes.

Arm IV: Single-agent Hormone Therapy. Stilphostrol or DES. (Arm terminated by 6/77 revision.)

Arm V: Radiotherapy. Irradiation of prostate, pelvic and para-aortic nodes. (Arm terminated by 6/77 revision.)

Arm VI: Radiotherapy. Irradiation of prostate, pelvic, para-aortic, mediastinal and supraclavicular nodes. (Arm terminated by 6/77 revision.)

STRATIFICATION BY: TNM staging system of AJCCS; histology: well-differentiated vs. poorly differentiated; surgery: radical resection vs. TUR vs. biopsy; status of lymph nodes: positive common iliac and/or para-aortic lymph nodes vs. positive pelvic lymph nodes, negative pelvic lymph nodes (as evaluated by lymphangiogram and/or laparotomy or unevaluated); method of lymph node evaluation: lymphangiography vs. laparotomy or not evaluated.

SPECIAL STUDY PARAMETERS: Acid phosphatase, rectal examination, plain film of abdomen, PA and lateral chest x-ray, IVP, bone scan, trans-rectal biopsy.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response as CR/PR and progression or no progression, direct extension, time to first metastases, loss of potency, urinary complications, rectal complications.

CURRENT STATUS: As of April 1980, 207 patients have been entered.

DOSAGE SCHEDULE:

Arm I:

Induction: Stilphostrol - total dose of 7 grams iv or im per week. Give Radiotherapy to each breast prior to Hormone therapy in order to minimize gynecomastia. Give 400 rads in 3 fractions over 3 days over each nipple using orthovoltage equipment.

Arm II: Radiotherapy - supervoltage, either cobalt-60, 2 MeV x-ray or 4 MeV linear accelerator. Pelvic node irradiation - total midplane dose of 4000 to 4500 rads in 4 to 5 1/2 weeks divided in fractions of 180-200 rads/day during 5 days/week.

Arm III: Radiotherapy - pelvic node irradiation as in Arm II. Para-aortic node irradiation - total midplane dose of 4800 rads.

Arm IV: Stilphostrol and DES as in Arm I with irradiation of each breast to minimize gynecomastia.

Arm V: Radiotherapy - pelvic and para-aortic irradiation as in Arm III with boost to prostate of total dose of 6500 to 7200 rads beginning on completion of the second 7- to 10-day period of rest. Split-course technique, or combination of a split course to the pelvis and nodal areas with continuous therapy to the prostate may be used at the option of an individual institution.

Arm VI: Radiotherapy - pelvic and para-aortic irradiation as in Arm III and mediastinal and supraclavicular irradiation - total midplane dose of 4000 rads divided into 170-200 rads/fraction for 4 to 5 days/week with techniques to assure that dose to supraclavicular nodes does not exceed 4000 rads. Booster dose to prostate as in Arm V.

Additional treatment - avoid TUR unless absolutely necessary. Treat patient with antibiotics, estrogens and/or radiation and attempt drainage before performing TUR.

Dosage modifications for radiation toxicity are given to minimize gynecomastia

Follow up once a month for initial 3 months during radiotherapy or hormonal therapy, then once every 3 months for months 4-12 and years 2 through 3, then once every 6 months for duration of survival.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/77

3.0053 RADIOTHERAPY USING NEUTRONS ALONE OR IN COMBINATION WITH PHOTONS FOR STAGE C ADENOCARCINOMA OF THE PROSTATE

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) RTOG-7704

OBJECTIVES:

I. Determine the efficacy of radiotherapy with fast neutrons alone, vs. mixed beam radiotherapy vs. radiotherapy with megavoltage photons in the treatment of Stage C adenocarcinoma of the prostate, as measured by relapse-free survival and total survival.

PROTOCOL ENTRY CRITERIA: Patients under 80 years of age with histologically proven Stage C adenocarcinoma of the prostate who have adequate bone marrow and renal functions. Patients must have a performance status of 40% or more on Karnofsky scale, and must not have had curative surgery or prior radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Neutron Therapy. Cyclotron neutron beam of 21.5 MeV or greater deuteron energy, or 14 MeV D-T neutron generator.

Arm II: Mixed Beam Therapy. Photon beam (4 MeV or greater, or Cobalt-60) plus neutrons (3 photon fractions/week plus 2 neutron fractions/week).

Arm III: Conventional Photon Radiotherapy.

STRATIFICATION BY: Histology: well vs. poorly differentiated; prior orchiectomy; presence of positive vs. negative pelvic lymph nodes as determined by lymphangiogram and/or laparotomy.

SPECIAL STUDY PARAMETERS: Rectal examination, chest x-ray, IVP, bone scan, trans-rectal biopsy, small bowel studies.

END POINTS: Response/remission rate, objective tumor response, lymph node response, time to first metastases, loss of potency, urinary complications, rectal complications, relapse-free survival, total survival.

CURRENT STATUS: 100-150 patients will be entered in 2-3 years.

DOSAGE SCHEDULE:

Arm I: Neutron therapy - 1000 rad equivalents/week given in 4 fractions.

Arm II: Mixed beam Radiotherapy - 1000 rad/week given in 3 photon and 2 neutron fractions.

Arm III: Photon therapy - 180-200 rad/day, 5 days/week.

For all arms give 5000 rad total midplane dose in 5 weeks to the pelvis with an additional 1500-2000 rad to the prostate, using reduced fields. A minimum dose of 6500 rad/6.5 weeks to 7000 rad/8 weeks should be delivered to the prostate.

Follow up all patients once a month for 3 months, then q 3 months through year 3, then q 6 months for life.

Dosage modifications for toxicity are not applicable.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00070478

3.0054 PROSTATIC IRRADIATION VS PELVIC IRRADIATION PLUS PROSTATE BOOST FOR STAGE A2 AND B PROSTATIC ADENOCARCINOMA

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PROTOCOL NUMBER(S) RTOG-7706

OBJECTIVES:

I. Determine the value of irradiation of the prostate only vs. pelvic irradiation with prostate boost in patients with Stages A2 and B adenocarcinoma of the prostate.

II. Compare the morbidity and complications of these two radiotherapeutic regimens.

PROTOCOL ENTRY CRITERIA: Patients with Stages A2 and B adenocarcinoma of the prostate who have not had potentially curable surgery and who have no evidence of lymph node metastasis on lymphangiogram. Patients with suspicious lymphangiograms may be admitted only if node biopsies are negative. Bone marrow and renal function must be adequate. Patients may not have had previous radiation therapy, except for skin cancer irradiated outside the present treatment fields, and there may be no previous or concurrent cancers other than skin cancer. Patients must have a Karnofsky performance status of at least 50 percent and may not be over the age of 80. There must be no history of multiple pelvic surgeries that would contraindicate pelvic irradiation.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Prostate irradiation. Megavoltage equipment with effective photon energies greater than 1 MeV or Co-60.

Arm II: Radiotherapy. Pelvic irradiation with prostate boost. Same equipment as in Arm I.

STRATIFICATION BY: Participating institutions, histology (Gleason Grades 1 and 2 vs. 3 and 4), prior endocrine therapy (estrogens or orchiectomy vs. no estrogens or orchiectomy), method of lymph node evaluation (lymphangiography vs. laparotomy).

SPECIAL STUDY PARAMETERS: Rectal examination, serum acid phosphatase, chest x-ray, IVP, bone scan, abdominal x-ray.

END POINTS: Survival, tumor response, lymph node status using lymphangiography, effectiveness of local control, time to first metastasis, loss of potency, urinary complications, renal complications.

CURRENT STATUS: 150 patients will be entered onto each arm over 24-30 months.

DOSAGE SCHEDULE:

Arm I: A minimum of 6500 rads in 6.5-7 weeks to the prostatic target volume, the maximum dose to any point within the target volume not exceeding 7200 rads, in daily fractions of 180-200 rads 5 days per week.

Arm II: A minimum of 4500-5000 rads to the whole pelvis target volume over 4.5-5.5 weeks, with an additional 1500-2000 rads to the local prostatic volume before, during, or after pelvic irradiation, using daily fractions of 180-200 rads and treating 5 days per week.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 08/80

3.0055 SEQUENTIAL VS CONCURRENT CHEMOTHERAPY WITH DIETHYLSTILBESTROL AND CYCLOPHOSPHAMIDE FOR STAGE IV PROSTATIC CARCINOMA

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PROTOCOL NUMBER(S) SEG-78PR0103; SEG-78PR342

OBJECTIVES:

I. Establish the objective response rate for cyclophosphamide (CTX) plus diethylstilbestrol (DES) therapy as initial treatment in the management of patients with Stage IV carcinoma of the prostate.

II. Compare the objective response rates, duration of response and survival of patients treated with DES/CTX given concurrently to those obtained when the same two drugs are given sequentially.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed metastatic prostatic carcinoma with at least one of the following conditions: measurable, soft tissue or pulmonary metastasis, elevated serum acid or alkaline phosphatase, any other measurable metastatic lesion. Patients must have had no prior hormonal or cytotoxic chemotherapy. Patients must have adequate hematologic status and not have any other malignant disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy plus Hormone Therapy. Cyclophosphamide, CTX, NSC-26271; Diethylstilbestrol, DES, NSC-3070.

Arm II: Sequential Single-agent Hormone Therapy plus Single-agent Chemotherapy. DES, CTX.

STRATIFICATION BY: Participating institutions, measurable vs. nonmeasurable disease.

SPECIAL STUDY PARAMETERS: Prostatic and bone marrow acid phosphatase, renal, hepatic, bone marrow functions.

END POINTS: Objective tumor response, duration of response, survival rate, length of response, toxicity/morbidity of treatment.

CURRENT STATUS: 160 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: CTX - 1000 mg/sqm iv on days 1 and 22; DES - 3 mg/day po in 3 divided doses. Evaluate 3 weeks after the second dose of CTX. Remove from study patients with progressive disease. Continue responders and stable patients on CTX - 1000 mg/sqm iv q 3 weeks; DES, as above.

Arm II: DES - 3 mg/day po continued until disease progresses; then begin CTX - 1000 mg/sqm iv q 3 weeks. After 6 weeks on CTX alone, remove from study patients with progressive disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 500 mg vials; DES - USP 1 mg tablets.

DATE SUMMARIZED: 10/78

3.0056 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE (DHAD) FOR ADVANCED PROSTATE CANCER

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-8010

OBJECTIVES:

I. Determine the response rate and remission duration in patients with prostate cancer treated with dihydroxyanthracenedione used in a single dose every-three-week schedule.

II. Define the qualitative and quantitative toxicities of dihydroxyanthracenedione administered in a Phase II study.

–PROTOCOL ENTRY CRITERIA: Patients with pathologically verified histologic diagnosis of prostate cancer. Disease must be measurable or evaluable. Patients must have failed on protocols of higher priority and be ineligible for higher priority SWOG protocols. A pretreatment WBC of 3000/cumm or greater and platelet count of 125,000/cumm or greater are required. Patients must be past the nadir resulting from prior therapy, particularly with nitrosoureas or mitomycin-C. Serum creatinine and bilirubin must be 2.0 mg percent or less and the patient's performance status must be 30-40 (Karnofsky) or better.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Participating institutions; prior chemotherapy: yes vs. no.

SPECIAL STUDY PARAMETERS: EKG; CAT; x-ray; hematologic, renal and hepatic function tests; tumor measurements.

END POINTS: Response/remission rate, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

DHAD - 10 mg/sqm through a free running iv over 30 minutes q 3 weeks for poor-risk patients; 12 mg/sqm for good-risk patients. Poor risk is defined as any of following: over 70 years of age, heavy prior chemotherapy or poor tolerance to prior chemotherapy, or radiotherapy to 25 percent or more of the bone marrow bearing areas. Patients who show progressive disease after 2 courses or those who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 5 mg ampules.

DATE SUMMARIZED: 10/80

3.0057 PHASE II HORMONE THERAPY WITH TAMOXIFEN FOR ADVANCED ADENOCARCINOMA OF THE PROSTATE

Nichols, W. C., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America

PROTOCOL NUMBER(S) MAYO-795201

OBJECTIVES:

I. Conduct a Phase II study of tamoxifen (TMX) for patients with advanced prostatic cancer who have failed a primary chemotherapy program or who are unsuitable candidates for cytotoxic treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of adenocarcinoma of the prostate, and histologic, x-ray/scan, or clinical evidence of metastatic disease outside the bed of the prostate (excludes patients with acid phosphatase elevation only). Patients must have measurable or evaluable disease (excludes palpation of prostate gland only), and must have failed a primary hormone program or be deemed ineligible for any higher order protocol. Patients must have progressed despite treatment with DES and/or orchiectomy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Hormone Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 20 patients will be treated unless an initial 11 consecutive failures are observed, in which case no further entries will occur. Accrual of patients should require 6-12 months.

DOSAGE SCHEDULE:

TMX - 40 mg/day in 2 divided doses po for 4 weeks, then every 8 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - tablets containing 15.2 mg Tamoxifen citrate, equivalent to 10 mg TMX.

DATE SUMMARIZED: 05/80

3.0058 PHASE II COMBINATION CHEMOTHERAPY WITH CAP (CTX/ADR/CDDP) AND CTX/CDDP FOR ADVANCED ADENOCARCINOMA OF THE PROSTATE

Nichols, W. C., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-795202

OBJECTIVES:

I. Assess the activity of combinations of cyclophosphamide (CTX) and cis-platinum (CDDP) with or without adriamycin (ADR) in patients with advanced prostatic cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of adenocarcinoma of the prostate, and histologic, x-ray/scan, or clinical evidence of metastatic disease outside the bed of the prostate (excludes patients with acid phosphatase elevation only). Patients must have measurable or evaluable disease (excludes palpation of prostate gland only), and must have failed a primary hormone program of orchiectomy and/or DES and be ineligible for any higher order protocol. Patients with certain clinical disorders and previous therapies will be excluded.

PROTOCOL OUTLINE: Nonrandomized study. Enter all patients with PS 0-2, who are less than 75 years old, with no active cardiac disease and with serum bilirubin less than 2 mg/dl in Regimen A. All patients 75 years or older, and/or with PS 3, and/or with active cardiac disease, and/or with serum bilirubin greater than 2 mg/dl will be entered into Regimen B.

Regimen A: 3-Drug Combination Chemotherapy. CAP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CDDP, NSC-119875.

Regimen B: 2-Drug Combination Chemotherapy. CTX; CDDP.

STRATIFICATION BY: Age, cardiac status, hepatic involvement, performance status.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, disease-free interval.

CURRENT STATUS: 20 patients will be entered to each regimen unless the first 14 in each fail to respond. Accrual will require 6-12 months.

DOSAGE SCHEDULE:

Regimen A: CAP: CTX - 400 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 1; CDDP - 40 mg/sqm iv on day 1. Repeat every 4 weeks. Patients with poor bone marrow reserve: CTX - 300 mg, ADR - 30 mg. Patients with creatinine 1.6-1.9: CDDP - 30 mg.

Regimen B: CTX - 900 mg/sqm iv on day 1; CDDP - 60 mg/sqm iv on day 1. Repeat every 4 weeks. Patients with poor bone marrow reserve: CTX - 750 mg. Patients with creatinine 1.6-1.9: CDDP - 45 mg.

Maintenance Regimen: CTX - 1000 mg/sqm iv on day 1. Repeat every 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; ADR - 10 and 50 mg vials; CDDP - 10 mg vials.

DATE SUMMARIZED: 05/80

3.0059 HORMONE THERAPY WITH TAMOXIFEN FOR METASTATIC ADENOCARCINOMA OF THE PROSTATE

von Eschenbach, A. C., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-325; MDA-U7901

OBJECTIVES:

I. Determine the effects of tamoxifen for untreated metastatic adenocarcinoma of the prostate and for metastatic adenocarcinoma of the prostate no longer responsive to estrogens and castration.

II. Correlate tumor responsiveness with presence or absence of estrogen and androgen protein receptor sites.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, metastatic adenocarcinoma of the prostate who have recovered from effects of major surgery and have had no other neoplasm in the previous 5 years. Patients must be previously untreated or refractory to prior therapy and castration. Patients must have an expected survival of at least 90 days and adequate hematologic function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Antiestrogen Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION: Participating institutions; prior therapy: previously untreated vs. relapsed or unresponsive to orchidectomy and estrogen.

SPECIAL STUDY PARAMETERS: Tumor response evaluation, estrogen and androgen protein receptor assays, prostate acid phosphatase, liver function, liver scan.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 60 patients will be entered in 2 years.

DOSAGE SCHEDULE:

TMX - 40 mg/day po in 2 divided doses for 12 weeks. Continue treatment indefinitely. Remove patients with disease progression from study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

3.0060 COMBINATION CHEMOTHERAPY WITH FAM (5-FU/ADR/MITO-C) ALTERNATING WITH FA (5-FU/ADR) FOR ADVANCED PROSTATIC CARCINOMA

vonEschenbach, A., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-407; MDA-U-8001

OBJECTIVES:

I. Evaluate the effectiveness of the combination FAM (5-fluorouracil/adriamycin/mitomycin-C) for patients with advanced prostatic carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed adenocarcinoma of the prostate who have failed on hormone therapy. Patients must have an expected survival of at least 90 days, adequate hematologic parameters, no history of another neoplasm except skin nonmelanoma, and no significant infection. Patients must have recovered from the effects of major surgery.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy alternating with 2-Drug Combination Chemotherapy. FAM: Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893; Mitomycin-C, MITO-C, NSC-26980; alternating with FA: 5-FU; ADR.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 15 evaluable patients will be entered.

DOSAGE SCHEDULE:

FAM: 5-FU - 750 mg/sqm on days 1 and 2; ADR - 50 mg/sqm on day 1; MITO-C - 10 mg/sqm on day 1. Patients receive 2 courses of FAM followed by alternating courses of FAM with FA: 5-FU and ADR, at same dosages as in the FAM combination.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

3.0061 CHEMOTHERAPY WITH ADR/CTX/CACP FOLLOWED BY ORCHIECTOMY FOR CHEMOTHERAPY FAILURES IN PATIENTS WITH METASTATIC PROSTATIC CARCINOMA

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PROTOCOL NUMBER(S) NCI-78-C-56; NCI-VA-MOB-778

OBJECTIVES:

I. Determine response rate and duration of response among patients with previously untreated metastatic adenocarcinoma of the prostate to aggressive combination chemotherapy with adriamycin/cyclophosphamide/cis-platinum.

II. Determine the efficacy of orchiectomy for patients who develop progressive disease on chemotherapy.

III. Investigate the utility of steroid hormone receptor protein determinations in predicting the response of prostatic cancer to hormone manipulation (and perhaps to combination chemotherapy) and study whether combination chemotherapy alters the presence or concentration of such proteins in individual patients.

IV. Study the effect of sequential chemotherapy and hormone therapy on various endocrinologic parameters and correlate any changes in these parameters with clinical response.

V. Investigate the utility of various serial staging procedures in detecting objective responses of this tumor to therapy, including lymphangiography, pelvic CAT scans, urinary hydroxyproline excretion, CEA, and bone marrow acid phosphatase measurements.

PROTOCOL ENTRY CRITERIA: Patients with pathologically confirmed adenocarcinoma of the prostate who have pathologically or radiographically documented extrapelvic metastatic disease and who have received no prior chemotherapy, hormone therapy, or radiotherapy to the pelvis or prostatic bed. Patients must be less than 70 years old and have a life expectancy of more than 2 months and a performance scale of 0-2. There may be no brain metastases or spinal cord compression. Hematologic, renal, hepatic, and cardiac function must be adequate. There may be no history of another malignant neoplasm within 5 years prior to entry, except for nonmetastatic skin tumor.

PROTOCOL OUTLINE: Nonrandomized study. Enter all patients on Regimen A. Enter patients who develop progressive disease on Regimen A to Regimen B.

Regimen A: 3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; cis-Platinum, CACP, NSC-119875; Mannitol, NSC-9256; Nitrogen Mustard, NM, NSC-762, as a substitute for CTX; 5-Fluorouracil, 5-FU, NSC-19893, as a substitute for ADR.

Regimen B: Surgery.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hemogram, SMA-12, acid phosphatase, 24-hour hydroxyproline excretion, EKG, creatinine clearance, audiogram, chest x-ray, testosterone, estradiol, DHEA, FSH, LH, bone scan, liver scan, IVP, metastatic bone survey, pelvic CAT scan, bone marrow biopsy and acid phosphatase, coagulation studies, lymphangiogram.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: ADR - 50 mg/sqm iv on day 1, total cumulative dose not to exceed 500 mg/sqm; CTX - 600 mg/sqm iv on day 1; CACP - 60 mg/sqm iv with prehydration and mannitol diuresis on day 1. Repeat courses q 21-28 days depending on recovery from myelosuppression. In the absence of significant myelosuppression after first course, escalate CTX to 800 mg/sqm. If less than 50 percent of CTX dose can be given because of toxicity, substitute NM at 8 mg/sqm iv on day 1. If ADR is discontinued for any reason, substitute 5-FU at 500 mg/sqm iv on days 1 and 2.

Regimen B: Orchiectomy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

3.0062 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED METASTATIC PROSTATIC CARCINOMA

Al-Sarraf, M., (312-494-6232) Wayne State University, School of Medicine, Department of Oncology, 3990 John R Street, Detroit, Michigan, 48201, United States of America
PROTOCOL NUMBER(S) WSU-C-31279

OBJECTIVES:

I. Determine the efficacy of AMSA in the treatment of measurable prostatic carcinoma.

II. Determine the toxicity of this agent.

PROTOCOL ENTRY CRITERIA: Patients with measurable, advanced prostate cancer. Patients with prior orchiectomy must have progressive disease. Patients must have a minimum life expectancy of 6 weeks and adequate hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: None given.

SPECIAL STUDY PARAMETERS: Hepatic and renal function, bone marrow and phosphatase.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: At least 25 patients to be entered over 8 to 10 months.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm (poor-risk patients - 65 years old or over with inadequate marrow reserve or hepatic function start at 100 mg/sqm) iv on day 1. Repeat course q 3 weeks. After 2 courses, patients with progressive disease are off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 02/80

3.0063 ADJUVANT IMMUNOTHERAPY WITH BCG FOR PROSTATIC CARCINOMA

Guinan, P., (312-633-6277) Cook County Hospital, Division of Urology, 1825 W. Harrison St., Chicago, Illinois, 60612, United States of America
PROTOCOL NUMBER(S) IL-PR-1

OBJECTIVES:

I. Evaluate the clinical effectiveness of adjuvant immunotherapy with BCG in prostatic carcinoma by means of a randomized trial.

PROTOCOL ENTRY CRITERIA: Patients with histologic diagnosis of prostatic carcinoma.

PROTOCOL OUTLINE: Randomized study.

Arm I: Conventional Therapy plus Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: Conventional Therapy alone (no details given)

STRATIFICATION BY: Clinical stage.

SPECIAL STUDY PARAMETERS: Leukocyte adherence inhibition assay.

END POINTS: Length of survival.

CURRENT STATUS: 70 patients entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: BCG - 2.6 x 10 to the eighth viable organisms, intradermal injection in left deltoid every 4 months, plus conventional therapy (dosage schedule not given).

Arm II: Dosage schedule not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - lyophilized, ampules.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 00700280

3.0064 RADIOTHERAPY VS HORMONE THERAPY WITH DES OR ORCHIECTOMY FOR STAGE C AND D1 CARCINOMA OF THE PROSTATE

Pater, J. L., (613-544-9580) National Cancer Institute of Canada, Clinical Trials Group, 12 O'Kill Street, Kingston, Ontario, K7L 5E2, Canada
PROTOCOL NUMBER(S) CAN-NCIC-PR1

OBJECTIVES:

I. Compare the effect of external megavoltage radiotherapy vs. standard hormone therapy (orchiectomy or diethylstilbestrol) on regression or spread of local disease, development of distant metastases, and survival in patients with Stage C or D1 prostatic cancer.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with histologically confirmed Stage C or D1 (T3 and T4, NX, N0, N1-N4, M0) adenocarcinoma of the prostate. There must be no evidence of distant metastases, and para-aortic nodes must be negative. Patients must have no significant concomitant disease and no history of another primary cancer (except basal or squamous cell carcinoma of the skin).

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Megavoltage irradiation of the pelvis.

Arm II: Hormone Therapy. Orchiectomy or Diethylstilbestrol, DES, NSC-3070.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Urinary function and potency, rectal examination, plasma testosterone, bone scan, cystoscopy, needle biopsy, renal and hepatic function tests.

END POINTS: Regression or spread of local disease, development of distant metastases, survival, objective tumor response, duration of response.

CURRENT STATUS: A total of 450 evaluable patients will be required.

DOSAGE SCHEDULE:

Arm I: 3600 rads to the prostate and pelvic lymph nodes over 3.5 weeks, with a boost of 2400 rads to the prostate over 2.5 weeks.

Arm II: Orchiectomy or DES - 3 mg/day in 3 divided doses, whichever is the local policy. (DES may be escalated to maintain plasma testosterone below 100 nanograms/ml.)

Patients who relapse continue treatment at the discretion of the physician; followup should continue.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

3.0065 COMPARATIVE STUDY OF HORMONE THERAPY WITH CTA, MPA, OR DES FOR ADVANCED PROSTATIC CANCER STAGE T3 AND T4

Macaluso, M. P., (Palermo 26-40-11) European Org. for Research on Treatment of Cancer, Genito-urinary Tract Cooperative Group, 9 Via Villa Tratoria, Palermo, Italy
PROTOCOL NUMBER(S) EORTC-30761; UICC-76091

OBJECTIVES:

I. Compare the effect of diethylstilbestrol (DES) vs. cyproterone acetate (CTA) vs. medroxyprogesterone acetate (MPA) on the objective response rate and the duration of remission in patients with advanced prostatic carcinoma.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with histologically proven Stage T3 or T4 carcinoma of the prostate. Patients must have adequate cardiac function.

PROTOCOL OUTLINE: Randomized study.

Arm I: Hormone Therapy. Cyproterone acetate, CTA, NSC-81430.

Arm II: Hormone Therapy. Medroxyprogesterone acetate, MPA, NSC-26386.

Arm III: Hormone Therapy. Diethylstilbestrol, DES, NSC-3070.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Bone scan/survey, chest X-ray, lymphography, plasma lipids, IVP, urethography, cystography.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of survival, objective tumor response, duration of remission, progression/relapse.

CURRENT STATUS: 279 patients will be entered.

DOSAGE SCHEDULE:

Arm I: CTA - 250 mg/day for 4 months continued to 1 year when possible.

Arm II: MPA - loading dose: 500 mg im 3 times weekly for 8 weeks. Maintenance period: 100 mg po twice daily.

Arm III: DES - 3 mg/day po for 4 months, continue as possible.

Evaluate patients in all Arms at 8 weeks. Continue therapy for complete and partial responders until progression. Treatment may be continued in patients with stable disease at investigator's discretion. Patients with progression go off-study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DES - 1 mg tablets.

DATE SUMMARIZED: 05/77

3.0066 COMPARISON OF SINGLE-AGENT HORMONE THERAPY WITH ESTRACYT VS DIETHYLSTILBESTROL FOR ADVANCED PROSTATIC CANCER, STAGE T3 AND T4

Lund, F., (Copenhagen 39.32.01) European Org. for Research on Treatment of Cancer, Genito-urinary Tract Cooperative Group, Copenhagen University School of Medicine, Copenhagen, Denmark
PROTOCOL NUMBER(S) EORTC-30762; UICC-76089

OBJECTIVES:

I. Compare the effect of diethylstilbestrol vs. estracyt on the objective response rate and the duration of remission in patients with advanced prostatic cancer.

PROTOCOL ENTRY CRITERIA: Patients with carcinoma of the prostate Stages T3 or T4 who have not received prior therapy other than trans-urethral resection of the prostate.

PROTOCOL OUTLINE: Randomized study.

Arm I: Hormonal Therapy. Estracyt, NSC-89199.

Arm II: Hormonal Therapy. Diethylstilbestrol, DES, NSC-3070.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum testosterone, perineal biopsy, Franzen needle biopsy, skeletal survey, urogram, bone scan, IVP.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of survival, objective tumor response, duration of remission.

CURRENT STATUS: About 186 patients will be entered in two years. (Reported January 1979 to enter more M1 patients in view of the problems of measuring prostatic tumors.)

DOSAGE SCHEDULE:

Arm I: Estracyt - 140 mg 2 x 2 daily po for eight weeks, then 280 mg/day in 2 divided doses for the rest of the study.

Arm II: DES - 3 mg/day (route not stated) given in three divided doses.

Continue therapy for responders until disease progression. Cross over nonresponders to alternate therapy for eight weeks and then discontinue treatment for nonresponders. Evaluate patients every six months and follow up until death.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/79

3.0067 PHASE II CHEMOTHERAPY WITH VINDESINE FOR REFRACTORY ADVANCED PROSTATIC CARCINOMA

Jones, W. G., (Leeds 673411) European Org. for Research on Treatment of Cancer, Genito-Urinary Tract Cancer Coop. Grp., Cookridge Hospital, Leeds LS16 6QB, United Kingdom
PROTOCOL NUMBER(S) EORTC-30799

OBJECTIVES:

I. Evaluate the effect of vindesine with respect to objective tumor response, the duration of any response, and the incidence and severity of side effects, in patients with advanced prostatic cancer for whom no other appropriate treatment is available either because of the advanced nature of the disease or because they have relapsed on or are resistant to conventional treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven advanced prostatic carcinoma, with measurable metastatic disease that is progressing. Patients (except those with histopathological Grade 3 tumors) must have failed on conventional therapy, and marker lesions for the objective assessment must be present (brain metastases, serous effusions, and sclerotic bone metastases are not acceptable). Patients must have an estimated survival time of 90 days and adequate hematologic function. Patients must have no second neoplasm (except skin non-melanoma), untreatable life-threatening diseases, psychiatric disorder, or bacterial infection. Patients must have received no previous treatment with vindesine and no radiotherapy, chemotherapy, or hormone therapy for 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: Stratification will be undertaken retrospectively.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; chest x-ray; rectal examination and estimate of prostate size.

END POINTS: Objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 27 patients have been entered as of December 1980. A total of 29 evaluable patients will be entered; the study will be discontinued if 3 or fewer responses are obtained.

DOSAGE SCHEDULE:

DAVA - 3.0 mg/sqm iv initial dose, increasing by 0.5 mg/sqm per week to a maximum dose of 4 mg/sqm per week (if toxicity allows). Treatment will be given weekly for 12 weeks; then the interval between injections is increased to a maximum of 3 weeks at the discretion of the observer. If progression occurs at any time after 6 weeks of treatment, the patient goes off the study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DAVA - 5 mg vials.

DATE SUMMARIZED: 10/80

3D. TESTIS

3.0068 PHASE III STUDY OF RETROPERITONEAL NODE SURGERY VS IRRADIATION FOR STAGE I NONSEMINOMATOUS TUMORS OF THE TESTIS

Carter, S. K., (415-497-7512) Northern California Oncology Group, 1801 Page Mill Rd., Bldg. B Suite 200, Palo Alto, California, 94304, United States of America
PROTOCOL NUMBER(S) NCOG-4T81

OBJECTIVES:

I. Compare the effects of surgery vs. radiation therapy on early testicular cancers with respect to the: disease-free interval, overall patient survival rate, patterns of relapse for failing patients, effect of chemotherapy tolerance in relapsing patients treated with systemic drug therapy, and relative treatment morbidity of the two modalities.

II. Describe the differences in disease-free rates and patterns of recurrence based upon histological subtypes, disease-free rates and patterns of recurrence between pathologic Stage I and II patients in the surgical group, role of tumor markers as monitors of disease activity, time course of tumor marker activity in response to surgery and radiotherapy, differences in disease-free rates or patterns of recurrence in patients with and without tumor marker activity, and accuracy of clinical staging by lymphangiography and computerized tomography in surgically treated patients.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed nonseminomatous pure or mixed malignant germ-cell tumors of the testis who have no clinical evidence of the disease following radical inguinal orchiectomy. Patients must have had no prior radiation therapy, cytotoxic chemotherapy nor major retroperitoneal surgery. Patients must have adequate hepatic, renal and bone marrow function and measured serum tumor markers. Patients must have no second malignancy except basal or squamous-cell skin carcinoma and must not have pure seminoma or pure choriocarcinoma.

PROTOCOL OUTLINE: Randomized study following orchiectomy.

Arm I: Surgery. Radical Retroperitoneal node dissection.

Arm II: Para-aortic and Ipsilateral Pelvic Node Radiotherapy. 4 MeV x-ray or betatron to the primary lymphatic drainage nodes of the testis including, for rightsided testicular tumors, the interaortocaval, precaval, paracaval, right common iliac, right external iliac nodes and right and left renal pedicules; for leftsided testicular tumors include the para-aortic, preaortic, left common iliac and left external iliac nodes.

STRATIFICATION BY: Tumor marker activity: elevated postorchiectomy vs. normal postorchiectomy; histological tumor type: pure vs. mixed germ-cell tumor.

SPECIAL STUDY PARAMETERS: Performance status; tumor marker activity: HCG and alpha fetoprotein; lymphangiogram; abnormal CAT scan; intravenous urography; chest stereography or tomography.

END POINTS: Disease-free interval, survival rate, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 100 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: Surgery. Remove all lymphatics, fatty and areolar tissue including right and left hilar nodes. Remove entire ipsilateral spermatic vessel; dissect area between common iliac arteries in front of the left common iliac vein.

Arm II: Radiation Therapy. 4500 rad to the central axis over a period of 6 weeks at 5 fractions/week. Maximum dose to each kidney 2000 rad; to spinal cord 4000 rad. Carefully shield opposite testicle.

Enter nonresponders to Chemotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 07/79

3.0069 COMBINATION CHEMOTHERAPY WITH CACP/VBL/BLEO WITH & WITHOUT LITHIUM CARBONATE NEUTROPENIA ATTENUATION FOR GERMINAL CELL TUMORS IN MALES

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PROTOCOL NUMBER(S) NCOG-4T82

OBJECTIVES:

I. Assess effect of addition of lithium carbonate to myelosuppressive combination chemotherapy with cis-platinum (CACP)/vinblastine (VBL)/bleomycin (BLEO) on infection rate, neutropenia, allowable dosage, remission, and survival for male patients with germinal-cell tumors.

PROTOCOL ENTRY CRITERIA: Male patients under 60 years of age with biopsy-proven germinal-cell tumors. Patients must have advanced disease (non-seminoma of at least stage N2 or M1, pure seminoma of stage M1, or non-resectable of any T or N stage) not curable by radiotherapy and/or surgery; relapsed disease after any treatment except chemotherapy with protocol drugs; or persistent elevation of malignancy markers after initial radiotherapy and/or surgery. Patients must have adequate kidney, liver, and thyroid function and normal salt and water intake.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. PVB: cis-Platinum, CACP, NSC-119875; Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066.

Arm II: 3-Drug Combination Chemotherapy plus Neutropenia attenuation. PVB; plus Lithium carbonate, NSC-16895.

STRATIFICATION BY: Participating institutions; previous therapy: none vs. radiotherapy vs. chemotherapy vs. radiotherapy plus chemotherapy; histological type: pure germ cell vs. mixed germ cell; stage: occult metastases vs. minimal disease vs. advanced pulmonary or advanced subdiaphragmatic vs. advanced pulmonary plus advanced subdiaphragmatic; Karnofsky performance status: 90 to 100 vs. 70 to 80 vs. 50 to 60; site of origin: testis vs. extragonadal.

SPECIAL STUDY PARAMETERS: Hematologic, liver, kidney, thyroid, and bone function; beta subunit HCG; alpha-fetoprotein; carcinoembryonic antigen; lung tomography; excretory urogram; lymphangiogram; liver size; testis and abdominal mass; adenopathy; and Karnofsky performance status.

END POINTS: Response/remission rate, duration of response, disease-free interval, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 114 patients in 3 years or 178 patients in 5 years.

DOSAGE SCHEDULE:

Arm I: PVB: CACP - 100 mg/sqm iv in 6 divided doses with prior and post hydration on day 1; VBL - 0.13 mg/kg (0.01 mg/kg increment for q 10 percent increase in Karnofsky status over 50) slow or push iv on days 1 and 2; BLEO - 15 mg/sqm (maximum cumulative dose 245 mg/sqm) slow or push iv on days 2, 8, and 15.

Arm II: PVB, as in Arm I; Lithium carbonate - 300 mg po twice a day on days 1 through 21.

Repeat cycle q 3 weeks. Continue therapy for 3 cycles after complete response. Give 4 cycles to patients with no measurable disease on initiation of chemotherapy. Give 3 additional cycles to patients who have undergone surgery for residual disease stable over 2 cycles of chemotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; VBL - 10 mg ampules; BLEO - 15 mg capsules; Lithium carbonate - 300 mg tablets.

DATE SUMMARIZED: 02/80

3.0070 PHASE II REINDUCTION CHEMOTHERAPY WITH VP-16/CACP/ADR/BLEO FOLLOWING PROGRESSION ON VBL MAINTENANCE FOR TESTICULAR CANCER

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PROTOCOL NUMBER(S) SEG-GU-P47

OBJECTIVES:

I. Determine the effects of chemotherapy with VP-16213 (VP-16)/cis-platinum (CACP)/adriamycin (ADR)/bleomycin (BLEO) for remission Reinduction in patients progressing on vinblastine (VBL) Maintenance of protocol SEG-78GU240 for disseminated testicular cancer.

PROTOCOL ENTRY CRITERIA: Patients treated on protocol SEG-78GU240 who have progressed on maintenance with VBL.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. VP-16213, VP-16, NSC-141540; cis-Platinum, CACP, NSC-119875; Adriamycin, ADR, NSC-123127; Bleomycin, BLEO, NSC-125066.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Pulmonary function, abdominal ultrasound and CAT scan, beta HCG, AFP.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 34 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Reinduction:

Give vigorous hydration with each course. Give normal saline 12 hrs before, during, and 12 hrs after CACP therapy.

VP-16 - 100 mg/sqm iv in 250 ml normal saline on days 1 through 5; CACP - 20 mg/sqm iv on days 1 through 5; ADR - 40 mg/sqm iv on day 1; BLEO - 30 units iv q week. Repeat course q 3 weeks for 4 courses.

Maintenance: VP-16 - 300 mg/sqm iv in 250 ml normal saline over 30 min q 4 weeks for 3 months for patients in complete remission and until progression for patients in partial remission or with stable disease. Remove from study patients with disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 and 25 mg vials; ADR - 50 mg vials; BLEO - 15 unit vials; VP-16 - 100 mg vials.

DATE SUMMARIZED: 11/79

3.0071 PHASE II CACP/VBL/BLEO WITH OR WITHOUT ADR INDUCTION CHEMOTHERAPY PLUS VBL MAINTENANCE FOR DISSEMINATED TESTICULAR CARCINOMA

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PROTOCOL NUMBER(S) SEG-78GU0102; SEG-78GU240

OBJECTIVES:

I. Define the value of standard induction remission with cis-platinum (CACP)/vinblastine (VBL)/bleomycin (BLEO) in disseminated testicular carcinoma on a multi-institutional basis.

II. Define the role of adriamycin (ADR) in combination with VBL/CACP/BLEO as a remission induction agent in disseminated testicular cancer.

III. Determine the qualitative and quantitative toxicity of the two regimens under study, and the value, if any, of maintenance VBL therapy in patients achieving complete remission.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven, disseminated, nonseminomatous testicular cancer not amenable to conventional surgery or Radiotherapy. Patients must never have suffered congestive heart failure nor have had prior Chemotherapy. Patient must have no other malignancy nor CNS disease refractory to Radiothrapy. Patients must have adequate renal function, a life expectancy over 4 weeks and a performance status greater than 40.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I: 3-Drug Combination Chemotherapy. PVB: cis-Platinum, CACP, NSC-119875; Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066.

Arm II: 4-Drug Combination Chemotherapy. PVB: CACP; VBL; BLEO; plus Adriamycin, ADR, NSC-12312.

Maintenance: Rerandomize responders to Arms III or IV.

Arm III: Single-agent Chemotherapy. VBL.

Arm IV: No treatment.

STRATIFICATION BY: Participating institutions; extent of disease: tumor surface area over 5 sqcm vs. less than 5 sqcm.

SPECIAL STUDY PARAMETERS: SMA-12, blood gases, pulmonary function, HCG beta subunit; alpha fetoprotein, abdominal ultrasound and CAT scans.

END POINTS: Objective tumor response, response rate, duration of remission, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: 68 patients will be entered within 2 years.

DOSAGE SCHEDULE:

Induction: Enter all patients within 23 days of diagnosis to Arms I or II.

Arm I: PVB: CACP - 20 mg/sqm iv on days 1 through 5 with adequate hydration; VBL - 0.15 mg/kg iv on days 1 and 2; BLEO - 30 Units iv on days 2, 9, and 16. Repeat course q 3 weeks for 4 courses.

Arm II: CACP, BLEO as in Arm I; VBL - 0.2 mg/g iv on day 2; ADR -50 mg/sqm iv on day 1. Repeat course q 3 weeks for 4 courses. For both Arms I and II patients perform a staging re-evaluation within 28 days of the last Induction course. Remove patients with progressive disease after 4 weeks and all patients with less than complete remission after 4 courses of therapy. Rerandomize patients in complete remission to Arms III or IV.

Maintenance:

Arm III: VBL - 0.3 mg/kg iv q 4 weeks for 20 weeks or until disease progresses.

Arm IV: No treatment.

Follow up all patients q month for 12 months, then q other month for 12 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; ADR - 50 mg vials; BLEO - 15 unit vials; VBL - 10 mg vials.

DATE SUMMARIZED: 10/78

3.0072 PHASE III LOW VS HIGH DOSE CACP PLUS VBL/BLEO FOLLOWED BY SURGERY & CTX/ACT-D/ADR/VBL MAINTENANCE FOR TESTICULAR GERM CELL NEOPLASMS

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PROTOCOL NUMBER(S) SWOG-7817

OBJECTIVES: (This protocol replaces SWOG-7610)

I. Determine in a randomized fashion the effectiveness of cis-diaminedichloro-platinum (CACP) given in the conventional low-dose daily schedule for 5 days versus high-dose intermittent treatment in remission induction of disseminated testicular cancer, when combined with vinblastine (VBL) and bleomycin (BLEO).

II. Determine the survival of patients who achieve a partial remission and are rendered disease-free by surgical removal of residual disease and maintained on the same chemotherapy as patients who achieved complete remission status on chemotherapy alone.

III. Determine the effectiveness of cyclophosphamide (CTX), actinomycin-D (ACT-D), adriamycin (ADR) and VBL in the maintenance of remission status.

IV. Document the nature and extent of the hematologic and nonhematologic side effects of the various drug combinations.

PROTOCOL ENTRY CRITERIA: Patients with metastatic testicular cancer of germinal cell origin. Patients must have measurable disease or elevated beta-HCG and/or alpha fetoproteins and an expected life span of 8 weeks or more. Patients must be free of CNS metastases and obstructive uropathy. Patients must have adequate hepatic, renal and bone marrow function and a performance status of 3 or better. Patients must not have prior treatment with the study agents and must be free of significant non-neoplastic lung pathology.

PROTOCOL OUTLINE: Randomized study, for Induction only.

Induction:

Arm I: 3-Drug Combination Chemotherapy. Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875 - low dose.

Arm II: 3-Drug Combination Chemotherapy plus Surgery. VBL; BLEO; CACP - high dose; followed by Surgery.

Maintenance. 4-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Actinomycin-D, ACT-D, NSC-3053; Adriamycin, ADR, NSC-123127; VBL.

STRATIFICATION BY: Histologic classification: seminoma, or embryonal carcinoma, yolk sac tumor, embryonal carcinoma plus seminoma and/or yolk sac tumor, or teratoma, embryonal plus teratoma with or without seminoma and/or yolk sac tumor, teratoma plus seminoma and/or yolk sac tumor, or choriocarcinoma, choriocarcinoma with any other; performance status: 0, 1 vs. 2, 3; participating institutions.

SPECIAL STUDY PARAMETERS: Hepatic, renal and bone marrow function; alpha fetoprotein; spirometry and diffusing capacity; audiogram; CAT scan or sonogram; beta-HCG radioimmunoassay.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, relapse free rate.

CURRENT STATUS: About 100 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Induction:

Arm I: VBL - 12 mg/sqm (7 mg/sqm if marrow reserve impaired) iv on day 1. Repeat q 28 days for 4 months; BLEO - 15 IU/sqm iv or im (maximum cumulative dose 200 IU/sqm) twice weekly until maximum dose is reached; CACP - 15 mg/sqm (10 mg/sqm if marrow reserve impaired) on days 1 through 5. Repeat q 28 days for 4 months.

Arm II: VBL - as in Arm I on day 1; BLEO - as in Arm I beginning on day 2; CACP - 120 mg/sqm (100 mg/sqm if marrow reserve impaired) iv on day 3. Administer CACP with mannitol diuresis. Repeat course q 28 days for 4 months. Evaluate all patients in Arms I and II q 2 months; if disease increases, remove patient from study. Surgery: 30 days after day 1 of last induction course, enter all partial responders and patients with stable disease for resection of all residual disease.

Maintenance: Enter all patients. Begin surgical patients after adequate recovery, 3 to 4 weeks postoperative. CTX - 750 mg/sqm (400 mg/sqm if marrow reserve impaired) iv on day 1; ACT-D - 1.2 mg/sqm (1 mg/sqm if marrow reserve impaired) iv on day 1 following CTX; ADR - 60 mg/sqm (45 mg/sqm if marrow reserve impaired; maximum cumulative dose 450 mg/sqm) iv on day 29; VBL - 12 mg/sqm (7 mg/sqm if marrow reserve impaired) iv on day 59. Repeat course q 3 months for 6 courses. Follow up all patients until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VBL - 10 mg vials; BLEO - 15 mg vials; CACP - 10 mg vials; ACT-D - 0.5 mg vials; CTX - 100, 200 and 500 mg ampules; ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 10/78

3.0073 SURGERY WITH OR WITHOUT VAB-V (VBL/ACT-D/CTX/BLEO/CACP) FOR STAGE II NON-SEMINOMATOUS, NON-CHORIOCARCINOMA TESTICULAR GERM CELL TUMORS

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PROTOCOL NUMBER(S) TCIS-TC-179/179R; EST-3878

OBJECTIVES:

I. Determine the effect of lymphadenectomy vs. lymphadenectomy plus combination chemotherapy with VAB-V: vinblastine/actinomycin-D/cyclophosphamide/bleomycin/cis-platinum for Stage II non-seminomatous, non-choriocarcinoma testicular germ cell tumors.

II. Define prognostic variables that may predict recurrence in patients with Stage I disease.

III. Define the effect of histological subtype and extent of disease at initial presentation on recurrence factors and disease-free rates.

IV. Evaluate the role of malignancy marker substances in early detection and in the management of recurrence, and determine the accuracy of lymphangiograms, CT scans, and ultrasound studies for staging of retroperitoneal nodal involvement.

PROTOCOL ENTRY CRITERIA: Patients between 15 and 65 years of age with histologically confirmed, Stage I or II, non-seminomatous, non-choriocarcinoma testicular germ cell carcinoma who have had a radical inguinal orchiectomy (scrotal is acceptable, but enter patient as having T-3 status). Patients must have adequate liver, kidney, and hematologic function and be free of disease in retroperitoneal area which precludes lymphadenectomy. Patients must not have had prior chemotherapy or radiotherapy.

PROTOCOL OUTLINE: Randomized study. Enter all Stage II patients to Surgery and then randomize to Arm I or II. Follow, but do not treat, patients with Stage I disease.

Induction:

Surgery. Extended retroperitoneal lymphadenectomy.

Arm I: No Chemotherapy.

Arm II: 5-Drug Combination Chemotherapy. VAB-V: Vinblastine, VBL, NSC-49842; Actinomycin-D, ACT-D, NSC-3053; Cyclophosphamide, CTX, NSC-26271; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Disease stage: tumor - T1 or T2 vs. T3; number of nodes: more vs. less than 5; extent of node involvement: N1 vs. N2a or N2b vs. N3.

SPECIAL STUDY PARAMETERS: Serum markers: beta HCG, AFP and LDH; lymphangiograms; ultrasound or CT scan; KUB; IVP; liver and pulmonary function; EKG, audiogram.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival time, survival rate.

CURRENT STATUS: About 200 patients will be entered in just over 2 years.

DOSAGE SCHEDULE:

Retroperitoneal node dissection preceded by bipedal lymphangiogram (or CT scan and ultrasound study). Randomize patients to Arms I or II, preferably within 2 to 4 weeks following surgery. Study entry up to 8 weeks is acceptable, if needed to recover from postsurgical complications.

Arm I: Observation only.

Arm II: VAB-V: VBL - 4 mg/sqm iv on day 1; ACT-D - 1 mg/sqm iv on day 1; CTX - 600 mg/sqm iv on day 1; BLEO - 30 mg/sqm iv push followed by 15 mg/sqm iv 24 hour infusion on days 1 through 6; CACP - 120 mg/sqm iv 1 hour infusion with mannitol diuresis on day 7. Repeat course at 28 days for a total of 2 courses.

Observe patients q month for the first year and q 2 months for the second year. Upon recurrence in patients from Arm I or II, give 2 courses of VAB-V followed, when they achieve complete remission, by maintenance with VBL - 4 mg/sqm iv on day 1, ACT-D - 1 mg/sqm iv on day 1; CACP - 40 mg/sqm iv 1 hour infusion on day 8. Repeat course q 4 weeks for 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ACT-D - 0.5 mg vials; BLEO - 15 IU ampules; CTX - 100, 200 and 500 mg vials; VBL - 10 mg ampules; CACP - 10 mg vials.

DATE SUMMARIZED: 10/79

3.0074 SURGERY WITH OR WITHOUT VBP CHEMOTHERAPY FOR STAGE II NON-SEMINOMATOUS, NON-CHORIOCARCINOMA TESTICULAR GERM CELL TUMORS

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PROTOCOL NUMBER(S) TCIS-TC-279/279R; SWOG-7990; SEG-TC-279; BCRP-7930

OBJECTIVES:

I. Determine the effect of lymphadenectomy vs. lymphadenectomy plus combination chemotherapy with VBP: vinblastine/bleomycin/cis-platinum for Stage II non-seminomatous, non-choriocarcinoma testicular germ cell tumors.

II. Define prognostic variables which may predict recurrence in Stage I disease.

III. Define the effect of histological subtype and extent of disease at initial presentation on recurrence factors and disease-free rates.

IV. Evaluate the role of malignancy marker substances in detection and management of recurrence, and determine the accuracy of lymphangiograms, CT scans, and ultrasound studies for staging of retroperitoneal nodal involvement.

PROTOCOL ENTRY CRITERIA: Patients between 15 and 65 years of age with histologically confirmed, Stage I or II, non-seminomatous, non-choriocarcinoma testicular germ cell carcinoma who have had a radical inguinal orchiectomy (scrotal is acceptable, but enter patient as having T-3 status). Patients must have adequate liver, kidney, and hematologic function and be free of disease in retroperitoneal area which precludes lymphadenectomy. Patients must not have had prior chemotherapy or radiotherapy.

PROTOCOL OUTLINE: Randomized study. Enter all Stage II patients to Surgery and then randomize to Arms I or II. Follow, but do not treat, patients with Stage I disease.

Induction:

Surgery. Extended retroperitoneal lymphadenectomy.

Arm I: No further treatment.

Arm II: 3-Drug Combination Chemotherapy. VBP: Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

STRATIFICATION: Disease stage: T1 or T2 vs. T3; number of nodes: more vs. less than 5; extent of involvement: N2 vs. N2a or N2b vs. N3.

SPECIAL STUDY PARAMETERS: Serum markers: beta HCG, AFP and LDH; lymphangiograms; ultrasound or CT scan; KUB; IVP; hematologic, kidney, liver and pulmonary function; EKG, audiogram.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival time, survival rate.

CURRENT STATUS: About 200 patients will be entered in just over 2 years.

DOSAGE SCHEDULE:

Retroperitoneal node dissection preceded by bipedal lymphangiogram (or CT scan and ultrasound study). Randomize patients preferably within 2 to 4 weeks following surgery. Study entry up to 8 weeks is acceptable if needed for recovery from postsurgical complications.

Arm I: Observation only.

Arm II: VBP: VBL - 0.15 mg/kg/day iv in 2 divided doses on days 1 and 2; BLEO - 30 U iv q 7 days; CACP - 20 mg/sqm iv on days 1 through 5. Repeat course at 4 weeks for a total of 2 courses. Give rigorous hydration.

Observe patients q month for the first year and q 2 months for the second year. Upon recurrence in patients from Arm I or II, give 4 courses of VBP followed, when they achieve complete remission, by Maintenance with VBL - 0.3 mg/kg iv q 4 weeks for 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VBL - 10 mg ampules; BLEO - 15 IU ampules, CACP - 10 mg vials.

DATE SUMMARIZED: 10/79

3.0075 CHEMOTHERAPY WITH VBL/BLEO AND INTRAVENOUS HYPERALIMENTATION FOR TESTICULAR CANCER

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PROTOCOL NUMBER(S) MDAR-148

OBJECTIVES:

I. Determine whether optimal nutritional support with intravenous hyperalimentation will enhance the tumor reductive effect of vinblastine/bleomycin chemotherapy in Stage III testicular cancer.

II. Determine whether the quality of life as determined by patient symptoms status, patient nutritional status, patient immune status and frequency of infectious complications and neuropathic complications is influenced by optimal nutritional support through intravenous hyperalimentation.

III. Determine whether optimal nutritional support with intravenous hyperalimentation will improve the complete response rate.

IV. Determine prospectively the immune status associated with response in the testicular cancer patient treated with vinblastine/bleomycin chemotherapy and observe if there is enhancement of the immune responses when optimal nutritional support with intravenous hyperalimentation is added to chemotherapy.

V. Determine the deleterious effect of vinblastine/bleomycin chemotherapy on the nutritional status in the control group and determine if intravenous hyperalimentation can prevent or reverse this effect.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven Stage III testicular cancer of any histological type including embryonal carcinoma; teratocarcinoma, either pure or mixed, choriocarcinoma and seminoma, pure.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy: Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066.

Arm II: 2-Drug Combination Chemotherapy: VBL and BLEO as in Arm I; plus intravenous hyperalimentation.

STRATIFICATION BY: Three categories of nutritional status; good or poor risk; embryonal carcinoma vs. other histology; minimal lung presentation vs. other Stage III presentations.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Not given.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Good-risk patients - VBL - 0.6 mg/kg split into 2 fractions iv on days 1 and 2. Initial total dose must not exceed 50 mg.

Poor-risk patients: 0.5 mg/kg iv on days 1 and 2. Initial total dose must not exceed 40 mg; BLEO - fixed total dose of 30 units per 24 hours iv infusion q 24 hours beginning on days 2 through 7.

Hospitalization for VBL/BLEO chemotherapy is required. Courses of chemotherapy are administered in back-to-back sequence during each hospitalization. Each back-to-back cycle of chemotherapy includes 2 courses of VBL/BLEO chemotherapy. The second course of each cycle of chemotherapy will be initiated during the same hospitalization when the absolute granulocyte count exceeds 2000, and total leukocyte count exceeds 4000, and gastrointestinal toxicity has resolved. The rest interval between each hospitalization for 2 courses of chemotherapy is 3 weeks.

Arm II: VBL, BLEO - as in Arm I. Hospitalization for VBL/BLEO chemotherapy is required. Hyperalimentation through subclavian vein catheters will begin the first day of each hospitalization for chemotherapy, will continue throughout both courses of chemotherapy scheduled for each hospitalization, and will terminate 24 hours before dismissal.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

3.0076 COMBINATION CHEMOTHERAPY WITH VBL/BLEO AND SEQUENTIAL CHEMOTHERAPY WITH CACP FOR ADVANCED TESTICULAR AND EXTRAGONADAL CANCER

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PROTOCOL NUMBER(S) MDAR-175

OBJECTIVES:

I. Determine the response rate of testis cancer patients with advanced presentations to vinblastine/continuous infusion bleomycin with sequential high-dose cis-platinum therapy.

II. Determine the response rate of testis cancer patients who have failed vinblastine/bleomycin to aggressive cis-platinum therapy with mannitol diuresis.

III. Determine the response rate of patients with advanced extragonadal primary neoplasia to vinblastine/continuous bleomycin with sequential high-dose cis-platinum therapy.

PROTOCOL ENTRY CRITERIA: Patients with extragonadal primary tumors of the anterior mediastinum or retroperitoneum and patients with advanced germinal cell testis cancer. Advanced germinal cell testis cancer presentations include any palpable abdominal mass, obstructive uropathy from tumor, mediastinal mass on chest roentgenogram, liver or GI tract involvement, inferior vena cava involvement. Minimal disease tumor presentations include gynecomastia without measurable tumor and pulmonary metastases less than 2.0 cm in greatest diameter with no more than 5 lesions per lung field. The minimal disease category shall receive initial therapy with vinblastine/bleomycin therapy only.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy plus Single-agent Chemotherapy. Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066; plus cis-Platinum, CACP, NSC-119875.

Arm II: Single-agent Chemotherapy. CACP.

STRATIFICATION BY: Advanced or minimal stage of disease.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, objective tumor response, biochemical evidence of tumor.

CURRENT STATUS: 20 patients will be entered.

DOSAGE SCHEDULE:

Arm I: VBL - 0.6 mg/kg divided equally into 2 fractions on days 1 and 2. BLEO - 30 units/1000 ml 5% g/DW/24 hours on days 2 through 7. Upon recovery from myelosuppression, usually during days 15 to 21, give DDP - 100 mg/sqm iv over 60-90 minutes. Mannitol given iv, and compazine given intramuscularly immediately prior to and following administration of CACP.

Arm II: CACP - 100 mg/sqm iv on days 1, 8 and 15.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

3.0077 HIGH-DOSE COMBINATION CHEMOTHERAPY WITH CTX/VP-16 PLUS IMMUNOTHERAPY WITH BMT AND MAINTENANCE WITH ADR/VP-16 FOR TESTICULAR CARCINOMA

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PROTOCOL NUMBER(S) MDAR-370; MDA-DT-7989

OBJECTIVES:

I. Determine if megadose chemotherapy with cyclophosphamide (CTX) and VP-16213 (VP-16) plus immunotherapy with bone marrow transfusions (BMT) can produce a higher and longer lasting remission in patients with testicular cancer who are refractory to front-line therapy or who relapse after initial response to front-line therapy.

II. Determine if megadose chemotherapy can produce a higher and longer lasting remission in patients with germinal tumors with an extragonadal primary and choriocarcinoma.

PROTOCOL ENTRY CRITERIA: Patients with: histologically proven testicular carcinoma who have failed front line therapy or relapsed after initial response; histologically proven testicular carcinoma with bulky disease who have unsatisfactory response to primary therapy, e.g., less than CR with significant residual disease; and terminal tumors with extragonal primary with unsatisfactory response to primary therapy, e.g., less than CR and significant residual bulky tumor. There must be no bone marrow involvement by tumor. Consideration will be given later to the use of this protocol for late intensification in CR for patients who are projected to have short response, e.g., extragonadal in CR, testicular in CR with initially extensive disease, significant choriocarcinoma elements and residual high HCG and AFP on remission. Patients must have life expectancy of 12 weeks, have measurable lesions, have been off chemotherapy and/or radiotherapy for 4 weeks prior to entry, and have recovered from toxicities resulting from previous therapy. They must be less than 60 years old and must understand that multiple aspirations of bone marrow are voluntary and are associated with the risk of general anesthesia. Patients with a history of myocardial disease or an abnormal EKG are ineligible, unless in the opinion of the investigator the risk of the disease outweighs the risk of high-dose Cytoxan and adriamycin cardiac toxicity.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 2-Drug Combination Chemotherapy plus Immunotherapy. Cyclophosphamide, CTX, NSC-26271; VP-16213, VP-16, NSC-141540, plus bone marrow transfusions (BMT).

Maintenance: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; VP-16.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: CMV serology; toxoplasmosis serology; EKG; abdominal ultrasound.

END POINTS: Response/remission rate, duration of response.

CURRENT STATUS: 20 patients will be admitted.

DOSAGE SCHEDULE:

Induction: CTX - 1.5 mg/sqm/day iv on days 1, 2 and 3; VP-16 - 200 mg/sqm/day iv on days 1, 2 and 3 in split doses of 100 mg q 12 hours; BMT on day 5. Repeat course when patient achieves full hematologic recovery from first course.

Maintenance: ADR - 40 mg/sqm on day 1; VP-16 - 50 mg/sqm/day on days 3, 4 and 5. Repeat for total of 4 courses.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

3.0078 CHEMOTHERAPY WITH CTX/VBL/ACT-D/BLEO/CACP PLUS SURGERY FOR DISSEMINATED NONSEMINOMATOUS GERM CELL TUMORS

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PROTOCOL NUMBER(S) MSKCC-7939

OBJECTIVES:

I. Increase the complete remission rate and shorten the duration of chemotherapy for disseminated nonseminomatous germ cell tumors with cyclophosphamide (CTX)/vinblastine (VBL)/actinomycin-D (ACT-D)/bleomycin (BLEO)/cis-platinum (CACP).

PROTOCOL ENTRY CRITERIA: Patients with Stage III or nonresectable Stage II nonseminomatous germ cell tumors of the testis. Patients must have no prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 5-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Vinblastine, VBL, NSC-49842; Actinomycin-D, ACT-D, NSC-3053; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

Enter partial responders to Surgery, complete responders to Maintenance.

Surgery: Remove residual tumor mass.

Reinduction: 5-Drug Combination Chemotherapy. CTX, VBL, ACT-D, BLEO, CACP.

Maintenance: 2-Drug Combination Chemotherapy. ACT-D, VBL.

STRATIFICATION BY: Disease stage, previous chemotherapy, participating institutions.

SPECIAL STUDY PARAMETERS: Lymphangiogram, IVP, beta subunit HCG, alpha-fetoprotein, CEA, liver scan, audiogram.

END POINTS: Response/remission rate.

CURRENT STATUS: 120 patients to be entered over 2 to 2.5 years.

DOSAGE SCHEDULE:

Induction: CTX - 600 mg/sqm iv on day 1; VBL - 4 mg/sqm iv on day 1; ACT-D - 1 mg/sqm iv on day 1; BLEO - 30 mg iv bolus on day 1; BLEO - 20 mg/sqm iv continuous infusion on days 1 through 3; CACP - 120 mg/sqm iv onday 4. Repeat q 3 to 4 weeks for 3 courses (omit BLEO on final course).

Surgery: Remove residual tumor. After surgery, enter Maintenance or begin 2 courses of Reinduction when residual tumor contained malignant elements. Patients with necrotic tumor or adult teratoma enter Maintenance.

Reinduction: CTX, VBL, ACT-D, BLEO, CACP as in Induction. Repeat for 2 courses (the first with BLEO and the second without), then enter Maintenance.

Maintenance: VBL - 6 mg/sqm iv on day 1; ACT-D - 1 mg/sqm iv on day 1. Repeat q 3 weeks for 9 to 12 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

3.0079 REDUCTIVE SURGERY PLUS CHEMOTHERAPY (CTX/VBL/ACT-D/BLEO/CACP) VS CHEMOTHERAPY ALONE FOR NONSEMINOMATOUS TESTICULAR TUMORS

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PROTOCOL NUMBER(S) NCI-77-C-25; NCI-MB-87

OBJECTIVES:

I. Determine whether surgical resection of all accessible tumor combined with chemotherapy (cyclophosphamide/actinomycin-D/bleomycin/vinblastine/cis-platinum) is more effective than chemotherapy alone in response induction and survival in patients with metastatic teratocarcinoma, embryonal carcinoma, infantile embryonal carcinoma, teratocarcinoma, or mixed tumors.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented metastatic germ cell tumors of the testis (embryonal carcinoma, infantile embryonal carcinoma, teratocarcinoma, or mixed tumor) with demonstrable metastases in or beyond the infradiaphragmatic lymph nodes or massive involvement of the retroperitoneal tissue. There must be metastases in sites accessible to resection. Patients must be under the age of 65 and must have adequate renal and pulmonary function. There must be no other major concurrent disease and no history of any other malignant disease except for adequately treated basal or squamous cell skin cancers. There may be no prior chemotherapy or radiotherapy and no documented massive hepatic and/or brain metastases.

PROTOCOL OUTLINE: Randomized study.

Arm I:

Induction: 5-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Vinblastine, VBL, NSC-49842; Actinomycin-D, ACT-D, NSC-3053; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

Maintenance: 4-Drug Combination Chemotherapy. CTX; ACT-D; VBL; CACP.

Arm II: Reductive Surgery plus 5-Drug Combination Chemotherapy. CTX; VBL; ACT-D; BLEO; CACP.

STRATIFICATION BY: Age (under vs. over 15 years), histology (teratocarcinoma with or without seminoma vs. embryonal carcinoma with or without seminoma vs. any of the above with elements of choriocarcinoma), extent of tumor (metastases in retroperitoneum only vs. beyond retroperitoneum).

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, CEA, B-HGG, AFP, 24-hour B-UCG, creatinine clearance, pulmonary function tests, chest x-ray, chest tomograms, IVP, liver scan, gallium scan, bone scan, audiogram.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 30 patients will be entered on each arm.

DOSAGE SCHEDULE:

Arm I: Induction: CTX - 650 mg/sqm iv on day 1; VBL - 4 mg/sqm iv on day 1; ACT-D - 1 mg/sqm iv on day 1; BLEO - 15 units/sqm iv infusion over 6 hours on days 1 through 7; CACP - 75 mg/sqm iv with prehydration and concurrent mannitol diuresis. Maintenance: CTX - 100 mg/sqm/day po on days 1 through 14; ACT-D - 1 mg/sqm iv on day 1; VBL - 4 mg/sqm iv on day 1; CACP - 25 mg/sqm iv on day 1 after hydration. Begin 3 weeks after beginning of Induction and continue at 3-week intervals for a total of 6 courses. Two weeks after the last Maintenance course give a second Induction identical to the original. Then administer 18 additional Maintenance cycles.

Arm II: Radical inguinal orchiectomy plus, depending on the site of metastases, retroperitoneal lymph node dissection and resection of pulmonary metastases. Initiate Chemotherapy as in Arm I, 2-4 weeks postoperatively.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

3.0080 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM/BLEOMYCIN/VINBLASTINE/VP-16 FOR ADVANCED NONSEMINOMATOUS TESTICULAR CARCINOMA

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PROTOCOL NUMBER(S) ARG-CMH-7806

OBJECTIVES:

I. Establish the toxicity of the drug combination Cis-platinum/Bleomycin/Vinblastine/VP-16 as well as the response rate and duration of response in patients with nonseminomatous carcinoma of the testis.

PROTOCOL ENTRY CRITERIA: Patients under 65 years of age with histologically confirmed, metastatic, measurable germ cell carcinoma of the testis, not pure seminoma. Elevated serum markers (alpha-fetoprotein, human chorionic gonadotropin) can be the major criterion of measurable disease. Patients must have adequate renal and pulmonary function, and must not have had prior chemotherapy with study drugs nor extensive prior radiotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction.

4-Drug Combination Chemotherapy. Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066; Cis-platinum, CACP, NSC-119875; VP-16, NSC-141540.

Maintenance.

Single-agent Chemotherapy. VP-16.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Bipedal lymphangiogram, alpha-fetoprotein, HCG, LDH.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of response, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction.

VBL - 0.1 mg/kg iv on days 1 and 2; BLEO - 15 mg/sqm (maximum cumulative dose 300 mg/sqm) 24-hour iv infusions on days 1, 2 and 3; CACP - 100 mg/sqm iv 20-hour infusion on day 4 with vigorous hydration; VP-16 - 50 mg/sqm iv on days 15, 17 and 19. Repeat course on day 29 and continue therapy until either complete remission, disease progression, or when marker levels double after adequate chemotherapy. Enter patients in complete remission to Maintenance.

Maintenance.

VP-16 - 75 mg/sqm iv on days 1, 3 and 5 q 28 days. Rebiopsy patients with predominantly teratocarcinoma who show only partial regression when disease is stable after 6 courses of chemotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/79

3.0081 CHEMOTHERAPY WITH BLEO/VBL/ACT-D WITH OR WITHOUT CIS-PLATINUM FOR STAGE III NON-SEMINOMATOUS CARCINOMA OF THE TESTIS

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PROTOCOL NUMBER(S) DAN-DATECA-6

OBJECTIVES:

I. Compare in a prospective randomized trial the effect of a four-drug regime (actinomycin-D, vinblastine, bleomycin and CACP) with a three-drug regime (actinomycin-D, vinblastine and bleomycin) in the treatment of previously untreated patients with NSCT Stage III testicular carcinoma.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with histologically diagnosed non-seminomatous carcinoma of the testis (NSCT) with proven distant metastases to lymph nodes above the diaphragm or to extranodal sites.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; Vinblastine, VBL, NSC-49842; Actinomycin-D, ACT-D, NSC-3053.

Arm II: 4-Drug Combination Chemotherapy. BLEO, VBL, ACT-D, plus cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Serum LH, FSH, beta-estradiol and alpha-fetoproteins, audiogram.

END POINTS: Objective tumor response, response/remission rate.

CURRENT STATUS: About 90 patients will be entered in three years.

DOSAGE SCHEDULE:

Arm I: BLEO - 7.5 mg/sqm iv on days 1 through 5; VBL - 6 mg/sqm iv on days 1 and 2; ACT-D - 2.5 mg/sqm iv on day 1. Repeat course q 4 weeks for 6 months and every 8 weeks for the subsequent 6 months.

Arm II: BLEO, VBL, ACT-D, as in Arm I; plus CACP - 20 mg/sqm iv on days 1 through 5. Repeat courses as in Arm I. Remove patients with confirmed objective progression from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ACT-D - 0.5 mg vials; VBL - 10 mg vials; BLEO - 15 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 04/78

3.0082 PHASE III INDUCTION CHEMOTHERAPY WITH CACP, VBL, BLEO FOR DISSEMINATED TESTICULAR NON-SEMINOMA

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PROTOCOL NUMBER(S) EORTC-30795

OBJECTIVES:

I. Investigate the therapeutic effectiveness of remission Induction chemotherapy with cis-platinum, vinblastine, and bleomycin, comparing the standard dose of vinblastine with a 25-percent reduction in the vinblastine dose.

II. Provide a remission Induction and Consolidation regimen for complete responders with a high speed of entry and with a low speed of entry into complete remission, in order to make them eligible for protocol 30796, where patients are randomized to Maintenance chemotherapy or no therapy.

III. Register, treat with chemotherapy, and follow those patients who have relapsed during or after radiotherapy on protocol 30791 or 30793, in order to determine which fraction of these patients will achieve complete remission, thereby establishing the relative merits of radiotherapy and chemotherapy in limited Stage II disease.

IV. Delineate prognostic features in patients on this regimen, considering type of histology, previous treatment, extent of tumor and tumor marker status, e.g. beta subunit chorionic gonadotrophin (B-HCG) and alpha-fetoprotein (AFP).

V. Register, treat with chemotherapy, and follow patients with Stage II teratoma trophoblastic.

PROTOCOL ENTRY CRITERIA: Patients with Stage III testicular non-seminoma or with malignant teratoma trophoblastic Stages II and III who have failed to respond to radiotherapy or chemotherapy or who show disease progression after such therapy, particularly those patients on the radiotherapy arm of protocol EORTC-30791 or 30793 who show progression. Patients must be under 65 years of age and have adequate bone marrow and renal function. Patients must have no second malignancy (except for basal cell skin cancer) and no previous chemotherapy with the protocol agents.

PROTOCOL OUTLINE: Study is randomized only with respect to dose level in Induction; patients are randomized to receive full dose or 75 percent of the full dose. Patients with prior Chemotherapy and/or Radiotherapy receive a dose level reduced by up to 50 percent. Patients with no evidence of metastatic disease after the fourth Induction cycle enter Consolidation.

Induction: 3-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Bleomycin, BLEO, NSC-125066; Vinblastine, VBL, NSC-49842.

Consolidation: 2-Drug Combination Chemotherapy. CACP; VBL.

STRATIFICATION BY: Prior therapy: yes vs. no; Stage III testicular non-seminoma vs. malignant teratoma trophoblastic Stages II and III.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; tumor marker status: LDH, B-HCG, AFP, chest x-ray; gamma-GT; pulmonary vital capacity measurement; audiogram.

END POINTS: Response/remission rate, elevated levels of tumor markers.

CURRENT STATUS: 40 patients have been entered as of June 1980. A total of 220 evaluable non-pretreated patients is required.

DOSAGE SCHEDULE:

Induction:

CACP - 20 mg/sqm iv with prehydration, mannitol diuresis and posthydration on days 1 through 5 q 3 weeks; BLEO - 30 mg iv in a 15-minute infusion on day 2, repeated weekly to a maximum cumulative dose of 360 mg; VBL - 0.2 mg/kg (full dose) iv bolus on days 1 and 2 of every cycle or 0.15 mg/kg (75 percent of full dose) or 0.1 mg/kg (for patients with previous Radio- and/or Chemotherapy) iv bolus on the same schedule. The second course cycle is started on day 22. Four cycles are given.

Consolidation:

CACP - 50 mg/sqm administered as per Induction on days 1 and 2, q 3 weeks; VBL - 0.2 mg/kg on days 1 and 2, q 3 weeks. Two courses are given.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

3.0083 MAINTENANCE CHEMOTHERAPY WITH CACP/VBL FOR TESTICULAR NON-SEMINOMA IN COMPLETE REMISSION

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PROTOCOL NUMBER(S) EORTC-30796

OBJECTIVES:

I. Compare the disease-free survival rates for Maintenance chemotherapy with vinblastine and cis-platinum with no Maintenance in patients in complete remission after remission Induction chemotherapy with cis-platinum, vinblastine and bleomycin on EORTC protocol 30795.

II. Define prognostic features in these patients, considering type of histology, previous treatment, extent of tumor, and tumor marker status such as beta-subunit chorionic gonadotrophin (beta-HCG) and alpha-fetoprotein (AFP).

III. Evaluate long-term nephrotoxicity of cis-platinum.

PROTOCOL ENTRY CRITERIA: Patients with Stage III testicular non-seminoma or with malignant teratoma trophoblastic Stage II and III who have achieved complete remission (verified by surgical exploration) after treatment on EORTC protocol 30795. Patients must have adequate renal and bone marrow function.

PROTOCOL OUTLINE: Randomized study. Patients who have achieved a complete remission on EORTC protocol 30795 are randomized for Maintenance 6 to 8 weeks after completion of EORTC protocol 30795 Induction Chemotherapy.

Maintenance:

Arm I: 2-Drug Combination Chemotherapy. Vinblastine, VBL, NSC-49842; cis-Platinum, CACP, NSC-119875.

Arm II: No further therapy.

STRATIFICATION BY: Prior therapy: 4 cycles of Induction on EORTC protocol 30795 vs. 4 cycles of Induction plus 2 cycles of Consolidation on EORTC protocol 30795; participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests, gamma-GT, B-HCG, AFP, chest x-ray.

END POINTS: Disease-free interval, toxicity/morbidity of treatment.

CURRENT STATUS: Six patients have been entered as of June 1980. A total of 152 patients will be entered and followed until death or relapse.

DOSAGE SCHEDULE:

Maintenance:

Arm I: VBL - 0.2 mg/kg iv bolus q 3 weeks; CACP - 50 mg/sqm iv with prehydration and posthydration q 6 weeks. Treatment is continued for 1 year.

Arm II: No treatment, followup for 4 years after entry.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

3E. GENITOURINARY—GENERAL

3.0084 PHASE III STUDY WITH CACP VS ADR/CTX/CACP & PHASE II STUDY WITH VM-26 FOR DISSEMINATED TRANSITIONAL CELL URINARY TRACT CANCER

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PROTOCOL NUMBER(S) EST-1878

OBJECTIVES:

I. Compare effect of single-agent chemotherapy with cis-platinum (CACP) to combination chemotherapy with adriamycin (ADR)/cyclophosphamide (CTX)/CACP for disseminated transitional cell carcinoma of the urinary tract.

II. Determine effect of VM-26 on this disease. (Closed to patient entry. Addendum 2, September 1980.)

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with measurable or evaluable, recurrent or metastatic transitional cell carcinoma considered incurable by radiotherapy or surgery. Patients must have adequate hematologic, renal, and hepatic function and a performance status less than 4. Patients must have recovered from the effects of prior treatment, which must not have included study drugs.

PROTOCOL OUTLINE: Randomized study. Assign patients with heart disease to Regimen A and patients with impaired renal function and those unwilling to continue therapy with cis-platinum to Regimen B. (Regimen B closed to patient entry. Addendum 2, September 1980.) Randomize all other patients to Arm I or II.

Arm I: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875; followed for nonresponders by CA: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

Arm II: 3-Drug Combination Chemotherapy. CAP-I (CAD): CACP; ADR; CTX.

Regimen A: 2-Drug Combination Chemotherapy. CD: CTX; CACP.

Regimen B: Single-agent Chemotherapy. VM-26, NSC-122819. (Closed to patient entry, September 1980.)

STRATIFICATION BY: Participating institutions; performance status: 0 and 1 vs. 2 and 3; measurable vs. evaluable disease; prior radiotherapy.

SPECIAL STUDY PARAMETERS: Ultrasonography.

END POINTS: Objective tumor response, duration of response, response/remission rate, survival time.

CURRENT STATUS: 160 patients will be entered to the Phase III trial in about 2 years; 30 patients will be entered to the Phase II trial (closed September 1980).

DOSAGE SCHEDULE:

Arm I: CACP - 60 mg/sqm iv given over 2 hours with furosemide hydration and mannitol diuresis q 3 weeks for 3 courses, then q 4 weeks for patients who demonstrate complete or partial response. Upon disease progression in these patients (as well as those who show no change or disease progression following the original 3 courses of Chemotherapy) give: CA: CTX - 400 mg/sqm iv q 3 weeks; ADR - 40 mg/sqm (total cumulative dose 450 mg/sqm) iv q 3 weeks.

Arm II: CAP-I (CAD): CTX - 400 mg/sqm iv; ADR - 40 mg/sqm iv; CACP - 60 mg/sqm iv with furosemide hydration and mannitol diuresis. Repeat course q 3 weeks for 3 courses, then q 4 weeks for patients who demonstrate complete or partial response. When a cumulative ADR dose of 450 mg/sqm is reached, discontinue this drug but continue CTX and CACP.

Regimen A: CTX - 1000 mg/sqm iv; CACP - 60 mg/sqm iv with hydration and diuresis. Repeat course q 3 weeks for 3 courses, then q 4 weeks for patients who demonstrate complete or partial response.

Regimen B: Enter all patients failing on Arm I, Arm II or Regimen A. VM-26 - 30 mg/sqm/day given iv over 1 hour for 5 days q 3 weeks for 3 courses. Continue Regimen B for patients who respond or show no change. (Regimen closed to patient entry, September 1980.)

Remove patients with disease progression from study. Give reduced starting doses to patients over 65 years of age and to patients with prior pelvic irradiation. Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200 and 500 mg vials; CACP - 10 or 25 mg vials; VM-26 - 50 mg vials.

DATE SUMMARIZED: 09/80

3.0085 CHEMOTHERAPY WITH MITOTANE PLUS HORMONE REPLACEMENT FOR ADRENAL CORTICAL CARCINOMA AND CHEMOTHERAPY WITH ADR FOR TUMORS UNRESPONSIVE TO MITOTANE

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PROTOCOL NUMBER(S) EST-1879

OBJECTIVES:

I. Measure response rates to moderate dose of mitotane in patients with well differentiated functioning adrenal cortical carcinomas.

II. Relate response rates to blood and urine levels of mitotane and its major metabolites.

III. Document incidence of toxicity in patients receiving mitotane and replacement with glucocorticoid and mineralocorticoid and relate toxicity to blood and urine levels of mitotane and its major metabolites.

IV. Measure response rates to adriamycin (ADR) in patients with well differentiated and/or functioning tumors unresponsive to mitotane.

V. Measure in a Phase II study response rates of patients with poorly differentiated and non-functioning adrenocortical carcinoma to ADR given as initial therapy.

PROTOCOL ENTRY CRITERIA: Patients between the ages of 18 and 75 with histologic diagnosis of adrenal cortex carcinoma. Patients must have measurable residual, recurrent or metastatic tumor in nonirradiated areas. ADR can be administered only to patients without history of heart failure or myocardial infarction within the previous 12 months. For patients receiving ADR the following criteria must be fulfilled: WBC greater than 4000; platelets greater than 100,000; BUN less than 20 mg percent; creatinine less than 1.5 mg percent; bilirubin less than 2 mg percent.

PROTOCOL OUTLINE: Nonrandomized study. Patients with well differentiated hormone- or nonhormone-producing tumors and those with poorly differentiated hormone-producing tumors enter Regimen A. Those with poorly differentiated nonhormone-producing tumors enter Regimen B, as do nonresponders to Regimen A.

Induction:

Regimen A: Single-agent Chemotherapy plus Hormone Replacement Therapy. Mitotane, NSC-38721, plus Cortisone Acetate, NSC-9703 and Fludrocortisone, NSC-11318.

Regimen B: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions; age; histologic diagnosis; response to therapy.

SPECIAL STUDY PARAMETERS: Mitotane toxicity; ADR toxicity: hematologic, gastrointestinal, liver and cardiovascular abnormalities.

END POINTS: Response rates, duration of response, toxicity, survival rate, length of survival.

CURRENT STATUS: 20 to 50 patients will be accessioned.

DOSAGE SCHEDULE:

Regimen A: Mitotane - 6 g daily in 3 divided doses; Cortisone acetate - 25 mg/day po; Fludrocortisone - 0.1 mg/day po. Response is assessed after 3 months. CR, PR, NC patients continue for another 3 months, after which Mitotane dosage is reduced to 3 g/day.

Regimen B: ADR - 60 mg/sqm iv q 3 weeks to total cumulative dose of 500 mg/sqm. Those with progressive disease go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 or 50 mg vials; Mitotane - not given.

DATE SUMMARIZED: 02/80

3.0086 PHASE II CIS-PLATINUM CHEMOTHERAPY WITH OR WITHOUT CTX/ADR FOR ADVANCED TRANSITIONAL CELL CANCER OF THE BLADDER, URETER, OR RENAL PELVIS

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PROTOCOL NUMBER(S) NBCP-6A

OBJECTIVES:

I. Evaluate cis-platinum (CACP) vs. CACP/cyclophosphamide (CTX)/adriamycin (ADR) for maximal effectiveness in the treatment of advanced urothelia (bladder, renal, pelvis, ureter) carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed measurable or evaluable metastatic lesions of transitional cell carcinoma of the renal pelvis, ureter or bladder or urethra. Patients must have adequate hematologic, renal, cardiac, and auditory functions and must have a life expectancy of more than 60 days. They must not have received prior antineoplastic chemotherapy and they must have recovered from the effects of prior surgery or radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: (Common Arm). Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: (Institutional Arm). 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; CACP.

STRATIFICATION BY: Prior cystectomy: yes vs. no.

SPECIAL STUDY PARAMETERS: SMA-12; if indicated: bone films or scan, lymphangiogram, IVP, CAT.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: At least 20 patients will be entered.

DOSAGE SCHEDULE:

Arm I: CACP - 70 mg/sqm iv q 3 weeks with mannitol diuresis and adequate hydration. Evaluate patients q 3 weeks.

Arm II.A. (MSKCC). CACP - 70 mg/sqm iv given in 5 to 15 minutes on day 1 q 3 weeks; CTX - 250 mg/sqm iv given in 1 to 5 minutes on day 2 q 3 weeks; ADR - 45 mg/sqm iv given in 1 to 5 minutes on day 3 q 3 weeks.

Arm II.B. (MDA). CACP - 100 mg/sqm iv given in 2 hours on day 2 q 3 weeks, using site #2, with mannitol diuresis and adequate hydration; CTX - 650 mg/sqm iv given in 15 minutes on day 1, using site #1; ADR -50 mg/sqm iv given in 15 minutes on day 1, using site #1.

Give a minimum of 2 courses, then continue therapy for responders or patients with stable disease. Remove patients with progressive disease from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; CACP - 10 mg vials; ADR - 10 and 25 mg ampules.

DATE SUMMARIZED: 05/79

3.0087 PHASE II HEXAMETHYLMELAMINE VS CIS-PLATINUM THERAPY FOR ADVANCED TRANSITIONAL CELL CANCER OF THE BLADDER, URETER, OR RENAL PELVIS

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PROTOCOL NUMBER(S) NBCP-6B

OBJECTIVES:

I. Assess the effect of cis-platinum (CACP) on metastatic or recurrent transitional cell carcinoma.

II. Determine the influence of oral hexamethylmelamine (HMM) on nonresectable or radiation recurrent transitional cell carcinoma

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed measurable or evaluable metastatic lesions of recurrent or nonresectable transitional cell carcinoma of the renal pelvis, ureter, bladder, or urethra. Patients must have adequate hematologic, renal, cardiac, and auditory functions and must have a life expectancy of more than 60 days. They must not have received prior antineoplastic chemotherapy and they must have recovered from the effects of prior surgery or radiotherapy.

PROTOCOL OUTLINE: Randomized study. Separately randomize patients with measurable vs. nonmeasurable disease.

Arm I: (Common Arm). Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: (Institutional Arm). Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

Cross over nonresponders to alternate therapy.

STRATIFICATION BY: Prior cystectomy: yes vs. no.

SPECIAL STUDY PARAMETERS: SMA-12; if indicated: bone films or scan, lymphangiogram, IVP, CAT, liver function tests.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CACP - 70 mg/sqm iv q 3 weeks with mannitol diuresis and adequate hydration. Evaluate patient q 3 weeks.

Arm II: HMM - 10 mg/kg/day po given in 4 divided doses for 21 days, followed by 7 days of rest. Repeat course q 4 weeks. Evaluate patients prior to each dose.

Give a minimum of 2 courses of Arm I, 1 course for Arm II, then continue therapy for responders or patients with stable disease. Cross over patients with disease progression or unacceptable toxicity to the alternate arm. Remove from study patients relapsing on the alternate therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: HMM - 100 mg capsules; CACP - 10 mg vials.

DATE SUMMARIZED: 05/79

3.0088 PHASE II VP-16 VS CIS-PLATINUM CHEMOTHERAPY FOR ADVANCED TRANSITIONAL CELL CANCER OF THE BLADDER, URETER, OR RENAL PELVIS

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PROTOCOL NUMBER(S) NBCP-6C

OBJECTIVES:

I. Evaluate VP-16 randomized against the common treatment arm of cis-platinum as treatment for patients with advanced measurable bladder, ureteral, and renal pelvis transitional cell cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed measurable or evaluable metastatic lesions of transitional cell carcinoma of the renal pelvis, ureter, bladder, or urethra. Patients must have adequate hematologic, renal, cardiac, and auditory functions and must have a life expectancy of more than 60 days. They must not have received prior antineoplastic chemotherapy and they must have recovered from the effects of prior surgery or radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: (Common Arm). Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: (Institutional Arm). Single-agent Chemotherapy. VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: Prior surgery: cystectomy vs. none; site of primary cancer: bladder vs. renal pelvis vs. ureter.

SPECIAL STUDY PARAMETERS: SMA-12; if indicated: bone films or scan, lymphangiogram, IVP, CAT.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival time, toxicity/morbidity of treatment

CURRENT STATUS: 30 patients will be entered in about 2 years

DOSAGE SCHEDULE:

Arm I: CACP - 70 mg/sqm iv q 3 weeks with mannitol diuresis and adequate hydration. Evaluate patient q 3 weeks.

Arm II: VP-16 - 125 mg/sqm iv on days 1, 3, and 5 q 5 weeks. Evaluate patient q 5 weeks.

Give a minimum of 2 courses of Arm I or Arm II, then continue therapy for responders or patients with stable disease. Cross over patients with disease progression after 2 courses to the alternate arm. Remove from study patients relapsing on the alternate therapy.

DOSAGE FORMS: CACP - 10 mg vials; VP-16 - 20 mg ampules.

DATE SUMMARIZED: 05/79

3.0089 PHASE II CHEMOTHERAPY WITH VP-16213 FOR INCURABLE OR METASTATIC CARCINOMA OF THE BLADDER AND PROSTATE

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PROTOCOL NUMBER(S) SEG-GU-P45

OBJECTIVES:

I. Define the optimum dose of VP-16213 (VP-16) in adult solid tumor patients.

II. Define the toxicity of VP-16 in these patients.

III. Determine the response rate of this agent in bladder and prostate cancer.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven unresectable or metastatic bladder cancer and Stage D prostatic cancer that has failed hormonal therapy. Patients must have a Karnofsky performance status of 50 or better and adequate renal and hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: SMA 12, bone scan.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: Approximately 68 patients will be entered in 36 months.

DOSAGE SCHEDULE:

VP-16 - 130 mg/sqm (patients with prior Radiotherapy begin at 100 mg/sqm) iv on days 1 through 3. Repeat course q 3 weeks until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VP-16 - 100 mg vials.

DATE SUMMARIZED: 02/80

3.0090 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE FOR METASTATIC MALIGNANCIES OF THE TESTES, BLADDER, PROSTATE AND KIDNEY

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PROTOCOL NUMBER(S) SWOG-7916

OBJECTIVES:

I. Determine the efficacy of gallium nitrate in patients with metastatic urological malignancies of the testes, bladder, prostate and kidney, who have failed on higher priority treatment protocols.

PROTOCOL ENTRY CRITERIA: Patients with incurable, measurable and histologically advanced metastatic testicular, bladder, prostate or kidney carcinoma who have failed a maximum of 2 carcinoma studies of higher priority or are ineligible for such trials. Patients must have a performance status better than 2 (Karnofsky 50-60), a life expectancy of 6 weeks, and adequate cardiac, renal, liver and hematologic function, and four weeks must have elapsed since cessation of prior chemotherapy or radiotherapy. (Patients with only one kidney are eligible, providing they meet special creatinine clearance criteria. Amendment 1, May 1980)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Gallium nitrate, NSC-15200.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Urine tests for creatinine clearance and quantitative proteins; audiograms; gallium scans; AFP and HCG for testicular patients; acid phosphatase for patients with tumors of the prostate.

END POINTS: Response rate, duration of survival, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: A minimum of 56 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Give all patients 2,000 ml of saline fluid on the night prior to chemotherapy and infuse 200 ml saline fluid/hour for 6 to 8 hours on day of treatment. Gallium nitrate - 700 mg/sqm infusion over 30 minutes in 200 ml N saline q 2 weeks. Repeat course if BUN is less than 20, creatinine is less than 1.2 and WBC and platelet counts are adequate. (Patients with one kidney must have BUN less than 30 mg percent, serum creatinine less than 1.5 mg percent (men) or 1.2 mg percent (women), and creatinine clearance greater than 60 cc/minute prior to retreatment. Amendment 1, May 1980) An adequate trial is 2 courses of therapy. Remove from study patients with disease progression, unsatisfactory stable disease or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Gallium nitrate - 100 mg ampules.

DATE SUMMARIZED: 11/79

3.0091 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED METASTATIC CARCINOMA OF THE GENITOURINARY TRACT

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PROTOCOL NUMBER(S) SWOG-7937

OBJECTIVES:

I. Determine the antitumor activity of AMSA, as determined by response rate, duration of response, and survival in patients with metastatic carcinoma of the genito-urinary tract who have failed on higher priority therapy.

II. Determine the nature and degree of toxicity of AMSA.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven, advanced metastatic renal pelvis transitional cell, bladder transitional carcinoma, prostatic adenocarcinoma or other malignancies of the ureter, testes or urethra not eligible for higher priority therapy. Patients must have a minimum life expectancy of 6 weeks and minimum Karnofsky performance status of 50 to 60. Patients must have adequate renal, hepatic and hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Single-agent Chemotherapy. AMSA, NSC-249992.

STRATIFICATION: Participating institutions; prior chemotherapy; prior therapy with adriamycin; risk: good vs. poor; disease type.

SPECIAL STUDY PARAMETERS: B-HCG, AFP.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival duration, toxicity/morbidity of treatment.

CURRENT STATUS: At least 75 patients to be entered.

DOSAGE SCHEDULE:

Regimen A: AMSA - 120 mg/sqm (poor-risk patients - over 65 years old, prior radiotherapy, impaired marrow reserve, or moderately impaired hepatic function - 90 mg/sqm; patients with severely impaired hepatic function - 75 mg/sqm to start) iv on day 1. Repeat course q 21 days or as toxicity permits. Remove patients with unacceptable toxicity or progressive disease after 2 courses. Follow all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 20 and 50 mg ampules.

DATE SUMMARIZED: 02/80

3.0092 PHASE II COMBINATION CHEMOTHERAPY WITH VP-16/CACP FOR ADVANCED TRANSITIONAL CELL CANCER OF THE BLADDER, URETER, AND RENAL PELVIS

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PROTOCOL NUMBER(S) MAYO-805101

OBJECTIVES:

I. Determine the antitumor activity of the combination VP-16213/cis-platinum in patients with measurable advanced transitional cell cancer of the bladder, ureter, and renal pelvis.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed transitional cell carcinoma of the renal pelvis, ureter, bladder, or urethra with evaluable metastases. Patients must meet one or more of the following measurable disease criteria: measurable skin or subcutaneous metastases, palpable and measurable lymph node metastases, metastatic pulmonary and/or mediastinal lesions by chest roentgenogram, biopsy-proven malignant hepatomegaly evaluable by physical examination and/or radioisotope scan, intra-abdominal disease demonstrable and measurable by computerized transaxial tomogram (CTT). There must be no more effective standard therapy available for disease characteristics. Patients must have a life expectancy of at least 60 days and a performance status of 2 or better. There must be adequate hematologic and renal function. The presence of another malignant neoplasm within the previous 10-year period (except for skin cancer other than malignant melanoma) or the presence of significant concurrent complication will preclude patient entry. Patients must have received no antineoplastic chemotherapy prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. VP-16213, VP-16, NSC-141540; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests, chest x-ray, LDH, CEA, bone scan, CTT, chemistry group.

END POINTS: Response/remission rate, objective tumor response, duration of response, length of survival.

CURRENT STATUS: Initially, 14 patients will be entered.

DOSAGE SCHEDULE:

VP-16 - 125 mg/sqm iv infusion over 30 minutes on days 1, 2, and 3; CACP - 70 mg/sqm iv infusion over 3 hours with pre- and posthydration and 25 g mannitol diuresis. Repeat course q 4 weeks. Responders continue treatment until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; VP-16 - 20 mg ampules.

DATE SUMMARIZED: 10/80

3.0093 PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE (AZQ) FOR ADVANCED GENITOURINARY CARCINOMA

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PROTOCOL NUMBER(S) MAYO-805501

OBJECTIVES:

I. Conduct a Phase II study of aziridinylbenzoquinone (AZQ) in patients with advanced genitourinary carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of prostatic, bladder, renal, or testicular carcinoma with histologic, x-ray/scan, or clinical evidence of metastatic disease. There must be measurable disease; for prostatic cancer, evaluable disease will be permitted. Patients must have an ECOG performance status better than 4 and adequate hematolologic, renal, and hepatic function. Patients must receive no chemotherapy within 4 weeks prior to entry (6 weeks for nitrosourea or mitomycin-C), no radiotherapy to more than 15 percent of the bone marrow within 4 weeks prior to entry, there must be no major surgery within 3 weeks prior to entry. Patients must have had no unrelated other active cancer in the 5 years prior to entry except non-melanoma skin epithelioma.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Aziridinylbenzoquinone, AZQ, NSC-182986.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; bone scan; bone x-rays; tumor measurement; tests needed to assess tumor status.

END POINTS: Response/remission rate, objective tumor response, clinical parameters.

CURRENT STATUS: For each tumor type, 15 patients will be entered.

DOSAGE SCHEDULE:

AZQ - 27.5 mg/sqm (22.5 mg/sqm for patients with prior chemotherapy or radiotherapy to more than 40 percent of the bone marrow) iv infusion over 5-15 min on day 1. Treatment is repeated at 4-week intervals-(interval may be prolonged up to 6 weeks based on hematologic or clinical parameters). Patients are treated until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZQ - 10 mg vials.

DATE SUMMARIZED: 01/81

3.0094 CHEMOTHERAPY WITH CACP VS CTX/ADR/CACP FOR METASTATIC TRANSITIONAL CELL CARCINOMA OF THE URINARY TRACT

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PROTOCOL NUMBER(S) MDAR-289; MDA-U7801

OBJECTIVES:

I. Determine the efficacy of a single agent chemotherapy with cis-platinum (CACP) vs. a 3-drug combination of CACP, cyclophosphamide (CTX) and adriamycin (ADR) in transitional cell carcinoma arising either in the renal pelvis, ureter or urinary bladder.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed transitional cell carcinoma of the renal pelvis, ureter or bladder with evaluable skin or lymph node metastases and metastatic lung or mediastinal lesions, and biopsy proven malignant hepatomegaly. Patients must have had no antineoplastic chemotherapy except intravesicular therapy, but may have had systemic immunotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy. CACP; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: Prior radiation therapy, bone marrow invasion.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 20 patients will be entered in Arm I in 1 year.

DOSAGE SCHEDULE:

Arm I: CACP - 70 mg/sqm iv on day 1 q 3 weeks.

Arm II: CACP - 100 mg/sqm iv on day 2; ADR - 50 mg/sqm iv on day 1; CTX - 650 mg/sqm iv on day 1. Reduce ADR to 40 mg and CTX to 550 mg in patients with prior extensive Radiotherapy or bone marrow invasion.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/78

3.0095 CHEMOTHERAPY WITH CIS-PLATINUM/CYCLOPHOSPHAMIDE/ADRIAMYCIN FOR NONRESECTABLE ADVANCED METASTATIC UROTHELIAL TUMORS

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PROTOCOL NUMBER(S) MSKCC-7818

OBJECTIVES

I. Determine the effect of cis-platinum/cyclophosphamide/-adriamycin on nonresectable epidermoid (transitional cell) carcinoma, squamous cell carcinoma and adenocarcinoma of the bladder, urethra, ureter, or renal pelvis metastatic to lung, lymph nodes, liver or subcutaneous sites.

PROTOCOL ENTRY CRITERIA: Patients with measurable, nonresectable epidermoid (transitional cell), squamous cell, or adenocarcinoma of the bladder, urethra, ureter, or renal pelvis metastatic to the lung, lymph nodes, liver or subcutaneous sites. Patients must have adequate renal function and be free of gross hearing deficit and recent history of cardiac irregularities.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Carcinoembryonic antigen, liver and CAT scan.

END POINTS: Objective tumor response, response/remission rate, duration of remission.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE: (Routes of drug administration are not given). CACP - 70 mg/sqm on day 1; CTX - 250 mg/sqm on day 2; ADR - 45 mg/sqm (maximum total dose 450 mg/sqm) on day 3. Repeat cycle q 3 to 4 weeks to a maximum of 10 cycles. Evaluate patients q 3 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

3.0096 MITOTANE AND/OR PHASE II CHEMOTHERAPY WITH CAP-I (CTX/ADR/CACP) FOR MAXIMALLY RESECTED ADRENOCORTICAL CARCINOMA

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PROTOCOL NUMBER(S) DUT-AZL-1

OBJECTIVES:

I. Determine the response rate and duration of response of treatment with mitotane (opDDD) at sufficiently high serum levels, starting shortly after radical or near radical tumor extirpation.

II. Determine the objective tumor response rate and duration of response of patients with adrenocortical carcinoma to combination chemotherapy with CAP-I - cyclophosphamide (CTX)/adriamycin (ADR)/cis-platinum (CACP) in a Phase II study of patients not responding to the opDDD therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven maximally resected adrenocortical carcinoma. Limited disease patients have no evident disease or have residual or metastatic tumor smaller than 2 cm in diameter. Consider all others extensive disease patients. Patients must have a Karnofsky performance status of 50 or better, no evidence of heart disease, creatinine clearance above 3 x 10 to the ninth power, a life expectancy better than 2 months and adequate hematologic function.

PROTOCOL OUTLINE: Nonrandomized study. Enter limited disease patients to Regimen A. Enter to Regimen B patients unresponsive to Regimen A and all patients with extensive disease.

Regimen A: Single-agent Chemotherapy. Mitotane, opDDD, NSC-38721.

Regimen B: 3-Drug Combination Chemotherapy. CAP-I: cis-Platinum, CACP, NSC-119875; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Audiogram, bone, liver and CAT scans, echography.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Enter patients with limited disease. opDDD - 1 g mixed with 16 g vegetable milk powder given 4 x/day po. Increase dosage if serum level has not reached about 25 mg/ml after 3 weeks. Re-evaluate tumor growth and hormonal production 2 months after reaching adequate serum level. If no adequate levels are reached after 4 months, or disease is progressing 2 months after adequate levels are reached of if patient has unacceptable side effects, cross over to Regimen B. Continue therapy for about 2 years for patients with stable or regressive disease. Follow up these patients q 3 months.

Regimen B: Enter patients with extensive disease and patients failing on Regimen A. CACP - 50 mg/sqm iv with adequate hydration and mannitol if needed; CTX - 600 mg/sqm iv bolus; ADR - 40 mg/sqm iv bolus (maximum cumulative dose 550 mg/sqm). Repeat course q 21 days for a minimum of 2 courses. Remove from study patients with tumor progression at 3 weeks after the second course. Continue therapy of patients with disease regression until relapse. Give 3 additional courses to patients with complete remission, then discontinue therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 09/79

SECTION 4

GYNECOLOGIC TUMORS

4A. CERVIX

EST-PC-879 PILOT STUDY OF DAG/CACP CHEMOTHERAPY FOR ADVANCED SQUAMOUS CANCER OF THE UTERINE CERVIX 4.0001
GOG-24 PHASE II RADIOTHERAPY VS RADIOTHERAPY PLUS IMMUNOTHERAPY WITH C. PARVUM FOR ADVANCED CERVICAL CARCINOMA 4.0002
GOG-7731 LOCAL EXCISION VS CRYOSURGERY FOR LIMITED GRADE 1, 2 OR 3 CERVICAL INTRAEPITHELIAL NEOPLASIA 4.0003
GOG-7732 SURGICAL CONIZATION VS CRYOSURGERY FOR EXTENSIVE GRADE 3 CERVICAL INTRAEPITHELIAL NEOPLASIA 4.0004
GOG-7831 PHASE III STUDY OF CIS-PLATINUM CHEMOTHERAPY DOSAGE SCHEDULES FOR ADVANCED CARCINOMA OF THE CERVIX 4.0005
GOG-7992 PILOT STUDY ON DOSE RANGE OF CHEMOTHERAPY WITH CTX/CACP FOR ADVANCED CERVICAL CARCINOMA 4.0006
GOG-7993 PILOT STUDY ON DOSE RANGE OF CHEMOTHERAPY WITH CACP/ADR FOR ADVANCED CERVICAL CARCINOMA 4.0007
NCOG-P-5C81 PHASE II SEQUENTIAL CHEMOTHERAPY WITH BLEOMYCIN/MITOMYCIN-C FOR RECURRENT OR METASTATIC SQUAMOUS CELL CARCINOMA OF THE CERVIX 4.0008
RTOG-7608 NEUTRON RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX 4.0009
RTOG-7906 PHASE I-II STUDY OF MISONIDAZOLE PLUS RADIOTHERAPY FOR STAGE IIIB OR IVA SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX 4.0010
RTOG-7920 PELVIC VS PELVIC PLUS PARA-AORTIC RADIOTHERAPY IN STAGE IIB OR BULKY IB, IIA CERVICAL CARCINOMA 4.0011
RTOG-8005 PHASE III RADIOTHERAPY WITH OR WITHOUT RADIOSENSITIZATION WITH MNI FOR STAGE IIIB AND IVA SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX 4.0012
SWOG-7936 PHASE II COMBINATION CHEMOTHERAPY WITH CACP VS MITO/CACP VS MITO/VCR/BLEO/CACP FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE CERVIX 4.0013
MAYO-796251 BLEO/CTX/ADR/CACP VS BLEO/CACP IN STAGE III-IV CERVICAL CARCINOMA WITH 5-FU/VCR/ADR/MITO OR 5-FU/VCR/MITO AFTER FAILURE 4.0014
MDAR-29 C. PARVUM IMMUNOTHERAPY, CHEMOTHERAPY WITH ADR AND RADIOTHERAPY FOR SQUAMOUS CARCINOMA OF THE CERVIX 4.0015
MDAR-30 SEQUENTIAL CHEMOTHERAPY WITH CTX, HMM, ADR FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE CERVIX 4.0016
MDAR-315 LARGE DOSE/FRACTION RADIOTHERAPY AND HYPOXIC CELL SENSITIZER MISONIDAZOLE FOR ADVANCED CARCINOMA OF THE UTERINE CERVIX 4.0017

MDAR-340 BLEOMYCIN/MITOMYCIN-C INDUCTION AND CYCLOPHOSPHAMIDE MAINTENANCE FOR RECURRENT SQUAMOUS CELL CARCINOMA OF THE CERVIX 4.0018
MDAR-409 COMBINATION CHEMOTHERAPY WITH CACP/ARA-C FOR SQUAMOUS CERVICAL CARCINOMA 4.0019
MSKCC-7977 CHEMOTHERAPY WITH BLEOMYCIN/CIS-PLATINUM FOR ADVANCED CERVICAL CANCER 4.0020
NCI-80-C-145 SURGERY PLUS ADJUVANT CHEMOTHERAPY WITH CACP/MITO/BLEO PLUS RADIOTHERAPY FOR CERVICAL CANCER WITH PARA-AORTIC LYMPH NODE DISEASE 4.0021
ARG-RNH-101 RADIOTHERAPY VS RADIOTHERAPY PLUS ADJUVANT IMMUNOTHERAPY WITH C. PARVUM FOR STAGE II CARCINOMA OF THE UTERINE CERVIX 4.0022
ARG-RNH-102 RADIOTHERAPY VS RADIOTHERAPY PLUS ADJUVANT IMMUNOTHERAPY WITH C. PARVUM FOR STAGE III CARCINOMA OF THE UTERINE CERVIX 4.0023

4B. OVARY

EST-PA-879 CACP/ADR/HMM ALTERNATING WITH CACP/ADR/HMM/C. PARVUM FOR STAGE III AND IV OVARIAN CANCER 4.0024
EST-PF-878 PILOT CHEMOTHERAPY WITH CHAD (CTX/HMM/ADR/CACP) PLUS RADIOTHERAPY FOR NONRESPONDERS WITH ADVANCED OVARIAN CANCER 4.0025
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GOG-25 PHASE II ADJUNCTIVE CHEMOTHERAPY WITH L-PAM PLUS IMMUNOTHERAPY WITH C. PARVUM FOR STAGE III EPITHELIAL CARCINOMA OF THE OVARY 4.0027
GOG-50 PHASE III POSTOPERATIVE CHEMOTHERAPY WITH ADRIAMYCIN FOR PRIMARY OR RECURRENT OVARIAN SARCOMA 4.0028
GOG-7862 PHASE III MELPHALAN CHEMOTHERAPY VS INTRAPERITONEAL RADIOACTIVE CHROMIC PHOSPHATE FOR STAGE I EPITHELIAL OVARIAN CANCER 4.0029
GOG-7863 PHASE II ADJUVANT CHEMOTHERAPY WITH VAC (VCR/ACT-D/CTX) FOR MAXIMALLY RESECTED GERM CELL TUMORS OF THE OVARY 4.0030
GOG-7864 PHASE III CHEMOTHERAPY WITH VBP (VBL/BLEO/CACP) AND VAC (VCR/ACT-D/CTX) FOR RECURRENT MALIGNANT GERM CELL TUMORS OF THE OVARY 4.0031
GOG-7891 PILOT CHEMOTHERAPY WITH MELPHALAN PLUS IMMUNOTHERAPY WITH LEVAMISOLE FOR STAGE III/IV OVARIAN CARCINOMA 4.0032
GOG-7961 PHASE III CHEMOTHERAPY WITH ADR/CTX VS ADR/CTX/CACP FOR ADVANCED OVARIAN ADENOCARCINOMA 4.0033
NCOG-5O83 PHASE I-II COMBINATION CHEMOTHERAPY WITH ADR/CTX PLUS RADIOTHERAPY AND SURGERY FOR OVARIAN CARCINOMA 4.0034
NCOG-5O91 AC (ADR/CTX) VS PAC (CACP/ADR/CTX) COMBINATION CHEMOTHERAPY FOR ADVANCED SURFACE EPITHELIAL CARCINOMA OF THE OVARY 4.0035
SWOG-7925 PHASE III INDUCTION AND MAINTENANCE WITH ADR/CTX/BCG VS ADR/CTX/CACP VS ADR/CTX/CACP/BCG FOR STAGE III AND IV OVARIAN CANCER 4.0036
BCRP-7924 COMBINATION CHEMOTHERAPY WITH CACP/ADR/CTX/VP-16 FOR STAGE III/IV OVARIAN CARCINOMA 4.0037
MAYO-806151 CHEMOTHERAPY WITH HCAP (CTX/ADR/CACP/HMM) VS CP (CTX/CACP) FOR STAGE III AND IV OVARIAN CARCINOMA 4.0038
MDAR-301 COMBINATION CHEMOTHERAPY WITH L-PAM/CACP VS HAC (HMM/ADR/CTX) FOR STAGES III AND IV EPITHELIAL OVARIAN CARCINOMA 4.0039
MDAR-64 SINGLE-AGENT THERAPY WITH L-PAM OR CACP AND COMBINATION CHEMOTHERAPY WITH HMM/CTX/ADR FOR ADVANCED CANCER OF THE OVARY 4.0040
MSKCC-7931 CHEMOTHERAPY WITH CTX, ADR, CACP, AND CLB FOR ADVANCED OVARIAN CARCINOMA 4.0041

OCSG-7601 CHEMOTHERAPY WITH L-PAM FOR SELECTED STAGE I AI OR BI OVARIAN CARCINOMA 4.0042
OCSG-7602 CHEMOTHERAPY WITH RADIOACTIVE CHROMIC PHOSPHATE VS L-PAM WITH OR WITHOUT RADIOTHERAPY FOR STAGE I AND II OVARIAN CANCER 4.0043
OCSG-7603 CHEMOTHERAPY WITH ACT-D/5-FU/CTX, MTX/CF/CTX, AND VCR/ADR, AND MTX/CF AND C. PARVUM IMMUNOTHERAPY FOR EPITHELIAL OVARIAN CARCINOMA 4.0044
SFCC-78070 COMBINATION CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE, ADRIAMYCIN AND CIS-PLATINUM FOR ADVANCED OVARIAN CARCINOMA 4.0045
WI-MCW-OV-1 POSTOPERATIVE RADIOTHERAPY PLUS MELPHALAN VS RADIOTHERAPY PLUS MELPHALAN PLUS BCG IMMUNOTHERAPY FOR OVARIAN CANCER 4.0046
WI-MCW-OV-2 POSTOPERATIVE MELPHALAN VS MELPHALAN PLUS BCG IMMUNOTHERAPY FOR STAGE III-IV OVARIAN CANCER 4.0047
CAN-NCIC-CG-7502 ADJUVANT RADIOTHERAPY, RADIOACTIVE CHROMIC PHOSPHATE AND MELPHALAN FOR LIMITED CARCINOMA OF THE OVARY 4.0048
CAN-NCIC-OV4 COMPARISON OF L-PAM VS L-PAM/HMM AFTER FAILURE ON ADR/CACP FOR STAGE III-IV OVARIAN CARCINOMA 4.0049
CAN-NCIC-7701 L-PAM VS HAM (HMM/ADR/L-PAM) CHEMOTHERAPY FOR RESIDUAL EPITHELIAL OVARIAN CANCER WITH CACP FOR NONRESPONDERS 4.0050
DUT-OV-1 SURGERY PLUS COMBINATION CHEMOTHERAPY WITH HEXA-CAF AND CHAP-5 FOR STAGE III AND IV OVARIAN CARCINOMA 4.0051
EORTC-16792 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED OVARIAN CARCINOMA 4.0052
EORTC-55772 L-PAM MAINTENANCE THERAPY WITH OR WITHOUT PRIOR POSTSURGICAL RADIOTHERAPY FOR EPITHELIAL CANCER OF THE OVARY, STAGES IC, IIB, & III 4.0053
EORTC-55775 SINGLE-AGENT CHEMOTHERAPY WITH BLEOMYCIN FOR OVARIAN CARCINOMA STAGES III AND IV 4.0054
EORTC-55803 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED OVARIAN CARCINOMA 4.0055
UICC-76034 CHEMOTHERAPY WITH CHLORAMBUCIL VS CHLORAMBUCIL PLUS HORMONE THERAPY WITH PROGESTIN FOR STAGES III AND IV ADVANCED OVARIAN CARCINOMA 4.0056
UICC-76077 ADJUVANT CHEMOTHERAPY WITH CLB OR HMM FOR EARLY OVARIAN CANCER 4.0057
UICC-78026 CHEMOTHERAPY WITH CTX/ADR/HEXAMETHYLMELAMINE VS CTX/ADR/CIS-PLATINUM FOR EPITHELIAL OVARIAN CANCER STAGES III AND IV 4.0058
UKM-OV-1 IMMUNOTHERAPY WITH NON-IMMUNE OR TUMOR-IMMUNE PIG LYMPH NODE CELLS FOR CARCINOMA OF THE OVARY 4.0059

4C. UTERUS

GOG-20 PROPHYLACTIC CHEMOTHERAPY WITH ADRIAMYCIN ADJUVANT TO SURGERY AND RADIOTHERAPY FOR STAGE I AND STAGE II UTERINE SARCOMAS 4.0060
GOG-7743 CHEMOTHERAPY WITH ADRIAMYCIN FOLLOWING SURGERY AND RADIOTHERAPY FOR ENDOMETRIAL CARCINOMA, STAGE I AND OCCULT STAGE II 4.0061
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SECTION 4

GYNECOLOGIC TUMORS

4A. CERVIX

4.0001 PILOT STUDY OF DAG/CACP CHEMOTHERAPY FOR ADVANCED SQUAMOUS CANCER OF THE UTERINE CERVIX

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PROTOCOL NUMBER(S) EST-PC-879

OBJECTIVES:

I. Define a tolerable regimen and determine the efficacy of dianhydrogalactitol (DAG) plus cis-platinum (CACP) for the treatment of advanced squamous cancer of the uterine cervix.

PROTOCOL ENTRY CRITERIA: Patients with evaluable or measurable histologgically diagnosed squamous cancer of the uterine cervix with disease beyond the pelvic area. Patients with disease confined to the pelvis are eligible if they have failed prior irradiation or their tumor is nonresectable. Patients must not have received former chemotherapy with DAG or CACP and must have adequate renal, bladder and hematologic function.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Dianhydrogalactitol, DAG, NSC-132313 given with Furosemide, NSC-269420, and Mannitol, NSC-9256; plus cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: SMA 6 and 12, creatinine clearance.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

CACP - 50 mg/sqm iv on day 1 following hydration and diuresis with Furosemide - 40 mg iv bolus and Mannitol - 12.5 gm iv bolus; DAG - 150 mg/sqm iv in a one-hour saline infusion on day 1 after CACP.

Repeat treatment q 21 days for at least 2 courses, then remove patients with progression from study. Continue treatment of all other patients until disease progression or prohibitive drug toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 or 25 mg vials; DAG - 50 mg vials

DATE SUMMARIZED: 10/79

4.0002 PHASE II RADIOTHERAPY VS RADIOTHERAPY PLUS IMMUNOTHERAPY WITH C. PARVUM FOR ADVANCED CERVICAL CARCINOMA

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United States of America
PROTOCOL NUMBER(S) GOG-24

OBJECTIVES:

I. Assess the therapeutic effectiveness of immunotherapy with intravenous C. parvum used concomitantly with radiotherapy in patients with advanced cervival carcinoma confined to the pelvis and/or para-aortic nodes.

PROTOCOL ENTRY CRITERIA: Patients with primary, nonrecurrent, previously untreated invasive squamous, adeno, mixed squamous and adeno, or adenosquamous carcinoma of the uterine cervix Stages IIB, IIIB, or IVA, who have no prior or concomitant malignancies at other sites excepting skin, and who if initially Stage IB clinically (Amendment, November 1978) on laparatomy do not evidence visceral or peritoneal metastasis. Patients must be free of preexisting significant hypertension, pulmonary compromise or autoimmune disease. Patients must have no severe GI symptoms, septicemia or severe infection. Wbc greater than 4,000, platelets greater than 150,000, as well as adequate liver and renal functions are required.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. X-ray generators which produce beams at peak photon energy of 1 MeV or more, or Cobalt-60 to the pelvis; optional intracavitary radiation therapy with radium, cesium or cobalt sources.

Arm II: Radiotherapy plus Immunotherapy. Radiotherapy as in Arm I; Corynebacterium parvum, C. parvum, NSC-220537.

STRATIFICATION BY: Participating institutions, clinical stage, and para-aortic node status.

SPECIAL STUDY PARAMETERS: Standard skin test antigens, total lymphocyte counts, T-cell counts, mitogen stimulation of lymphocytes.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 150 patients will be entered per year for 2 years.

DOSAGE SCHEDULE:

Arm I: Begin radiotherapy no sooner than 2 weeks and no later than 6 weeks following staging surgery (Amendment August 1978). For stage IIIB and IVA, deliver external radiotherapy of 5000-6000 rads to the pelvis over 6 to 8 weeks, with optional intracavitary implant therapy of 2000 to 3500 rads during or following external radiotherapy, but no later than 2 weeks following, with total elapsed time for completion of both not to exceed 10 weeks. For Stage IIB, deliver external therapy of 4000 rads over 4 to 5 weeks with intracavitary dose of 4000 rads to point 'A' during or following completion of external therapy, and with maximum total elapsed time for both at 10 weeks.

Arm II: (Amendment, August 1978). Radiotherapy as in Arm I; C parvum - 4 mg/sqm iv infusion beginning within 6 weeks of day of surgery. Give the second dose 5 days later and thereafter q 2 weeks during radiotherapy and then 6 months for a total of 1 year. Discontinue on hypersensitivity to mercury or merthiolate.

DOSAGE FORMS: C. parvum - 1 ml ampules.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 01160179

4.0003 LOCAL EXCISION VS CRYOSURGERY FOR LIMITED GRADE 1, 2 OR 3 CERVICAL INTRAEPITHELIAL NEOPLASIA

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PROTOCOL NUMBER(S) GOG-7731, GOG-31

OBJECTIVES:

I. Evaluate and compare the immediate and long-term effectiveness of outpatient cryosurgery and outpatient local excision in the treatment of limited cervical intraepithelial neoplasia Grades 1, 2 or 3.

PROTOCOL ENTRY CRITERIA: Nonpregnant patients with histologically confirmed Grades 1, 2 or 3 cervical intraepithelial neoplasia (CIN) diagnosed within 6 weeks of study entry and which can be completely delineated through the colposcope and involves only one quadrant of the portio. Delineate ectocervical distribution by Lugol's staining. Endocervical curettage must be negative for CIN and microinvasive or invasive carcinoma. Patients must not have had previous or concomitant genital malignancy, or previous pelvic irradiation.

PROTOCOL OUTLINE: Randomized study.

Arm I: Cryosurgery. Perform in outpatient clinic with nitrous oxide (NO) or carbon dioxide (CO2) as a refrigerant at minus 65 degrees Centigrade to minus 85 degrees Centigrade.

Arm II: Surgical Excision. Perform in outpatient clinic by colposcopically directed sharp excision of the area as delineated by Lugol's solution and acetic acid.

Follow up all patients at 4 and 8 months post-therapy, semiannually for the remainder of the first 2 years and annually for the next 3 years.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Cervical cytology, Pap smear, pelvic exam, colposcopy, colpophotographs.

END POINTS: Recurrence free interval, survival rate, incidence and severity of complications.

CURRENT STATUS: 600-750 patients will be entered in 2-2.5 years.

DOSAGE SCHEDULE: Not applicable.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 01060179

4.0004 SURGICAL CONIZATION VS CRYOSURGERY FOR EXTENSIVE GRADE 3 CERVICAL INTRAEPITHELIAL NEOPLASIA

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PROTOCOL NUMBER(S) GOG-7732; GOG-32

OBJECTIVES:

I. Compare the immediate and long-term effectiveness of outpatient cryosurgery to the standard cold-knife conization in the treatment of extensive cervical intraepithelial neoplasia (CIN) in a Grade 3 randomized, prospective study.

PROTOCOL ENTRY CRITERIA: Nonpregnant patients with histologically confirmed Grade 3 cervical intraepithelial neoplasia that can be completely delineated through the colposcope and that involve at least two quadrants of the portio (with at least one quadrant diagnosed as CIN 3 - Addendum January 1980). Patients must not have had previous pelvic irradiation or treatment for CIN.

PROTOCOL OUTLINE: Randomized study.

Arm I: Outpatient Cryosurgery.

Arm II: Surgical Conization.

Evaluate patients at 4 and 8 months post-therapy, q 6 months for the remainder of the first 2 years post-therapy and then once q year for the next 3 years.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Cervical cytology, Pap smear, pelvic examinations, colposcopy, colpophotographs, endocervical curettage, directed biopsies.

END POINTS: Recurrence-free interval, surgical complications rate and severity, survival time, survival rate.

CURRENT STATUS: 300 patients will be entered in one year.

DOSAGE SCHEDULE: Not applicable.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00210179

4.0005 PHASE III STUDY OF CIS-PLATINUM CHEMOTHERAPY DOSAGE SCHEDULES FOR ADVANCED CARCINOMA OF THE CERVIX

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PROTOCOL NUMBER(S) GOG-7831; GOG-43

OBJECTIVES:

I. Confirm the effectiveness of cis-platinum (CACP) in advanced and recurrent squamous cell carcinoma of the cervix no longer responding to radiation therapy or surgery.

II. Compare the frequency and duration of response, and adverse effects of CACP therapy using three different doses and treatment schedules.

III. Evaluate the serial determination of serum carcinoembryonic antigen (CEA) levels in determining extent of disease, response to treatment, and in predicting treatment failure.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable or evaluable locally advanced, recurrent, persistent or metastatic squamous cell carcinoma of the cervix resistant to surgical treatment or radiotherapy. Patients must have a GOG performance scale of grade 0, 1, 2 or 3 (Karnofsky scale 30 to 100). Patients must have adequate hematological and renal function and must have had no prior chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I, II and III: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875; plus Furosemide, NSC-269420; and Mannitol, NSC-9256 as needed.

Arm I: Low-dose, q 3 weeks.

Arm II: High-dose, q 3 weeks.

Arm III: 5-day schedule, q 3 weeks.

STRATIFICATION BY: Performance: 0-1 vs. 2-3; measurable disease in pelvis vs. extra-pelvic recurrence; measurable disease vs. abnormal CAT scan.

SPECIAL STUDY PARAMETERS: Kidney function tests: BUN, creatinine, creatinine clearance, Ca, K, alkaline phosphatase; CAT scan; IVP; CEA; pretreatment audiogram (Amendment July 1979).

END POINTS: Response/remission rate, disease-free interval, toxicity/morbidity of treatment, duration of survival, survival rate, objective tumor response.

CURRENT STATUS: 175 patients per year will be entered in 2 1/2 to 3 years.

DOSAGE SCHEDULE:

Arm I: CACP - 50 mg/sqm iv at the rate of 1 mg/min given q 3 weeks for 8 courses with adequate hydration. Cross over patients who progress before 8 courses to Arm II.

Arm II: Hospitalize all patients. Pretreat patients with Mannitol and Furosemide. CACP - 100 mg/sqm infused iv at the rate of 1 mg/min given q 3 weeks for 4 courses.

Arm III: CACP - 20 mg/sqm iv infused at a rate of 1 mg/ml on days 1 through 5 q 3 weeks for 4 courses.

Patients showing progression before total CACP dose of 400 mg/sqm are off study, as are those showing excess toxicity. Discontinue CACP after a total cumulative dose of 400 mg/sqm in patients who achieve tumor stabilization or regression. (If tumor progression after total dose of 400 mg/sqm is observed, eligible patients may be retreated. Addendum, July 1979.

Dosage modifications for toxicity and eligibility criteria for retreatment with CACP (Addenda July 1979 and January 1980) are given.

DOSAGE FORMS: CACP - 10 and 50 mg vials.

DATE SUMMARIZED: 04/80

4.0006 PILOT STUDY ON DOSE RANGE OF CHEMOTHERAPY WITH CTX/CACP FOR ADVANCED CERVICAL CARCINOMA

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PROTOCOL NUMBER(S) GOG-7992

OBJECTIVES:

I. Determine dose range and toxicity of combination chemotherapy with cyclophosphamide (CTX)/cis-platinum (CACP).

II. Determine objective and subjective response of patients with advanced squamous cell carcinoma of the cervix.

PROTOCOL ENTRY CRITERIA: Patients between 18 and 75 years of age with histologically-confirmed, locally advanced, recurrent, persistent, or metastatic, squamous cell carcinoma of the cervix that is resistant to curative treatment with surgery or radiotherapy. Patients must have: GOG performance status of at least 3, normal renal function, and adequate hematologic function. Patients must not have had previous chemotherapy, radiotherapy in prior 3 weeks, extended field radiation, or previous (other than skin) cancer; they must not have clinically significant infection.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Kidney, liver, and hematologic function; electrolytes; tumor measurement; pelvic findings; performance status; audiometry.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

Enter 2 successive cohorts of 3 evaluable patients without prior surgical exploration or pelvic radiation to: CTX - 500 and 750 mg/sqm; CACP - 100 mg/sqm (concentration of 1 mg/ml) with 4 hrs prior and 12 hrs post hydration including furosemide and mannitol. Enter all additional patients to CTX - 1000 mg/sqm; CACP - 100 mg/sqm. Enter 3 successive cohorts of 3 evaluable patients with prior surgical exploration or pelvic radiation to: CTX - 500, 750, and 875 mg/sqm; CACP - 100 mg/sqm. Enter all additional patients to CTX - 1000 mg/sqm; CACP - 100 mg/sqm. Give all drugs iv (1 ml/min for CACP) q 3 weeks. After one course of therapy, continue until progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; CACP - 10 and 50 mg vials.

DATE SUMMARIZED: 02/80

4.0007 PILOT STUDY ON DOSE RANGE OF CHEMOTHERAPY WITH CACP/ADR FOR ADVANCED CERVICAL CARCINOMA

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PROTOCOL NUMBER(S) GOG-7993

OBJECTIVES:

I. Determine dose range and toxicity of combination chemotherapy with cis-platinum (CACP)/adriamycin (ADR).

II. Determine objective and subjective response of patients with persistent or recurrent squamous cell carcinoma of the cervix.

PROTOCOL ENTRY CRITERIA: Patients up to 75 years of age with histologically-confirmed, persistent or recurrent, squamous cell carcinoma of the cervix. Patients must have: GOG performance status of at least 3, normal renal function, and adequate hematologic function. Patients must not have: radiotherapy in prior 3 weeks or extended field radiation.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Kidney, liver, and hematologic function; electrolytes; tumor measurement; pelvic findings; performance status.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

Enter successive cohorts of 3 evaluable patients. First cohort: ADR - 30 mg/sqm; CACP - 100 mg/sqm (concentration of 1 mg/ml) with 4 hours prior- and 12 hours post-hydration including furosemide and mannitol. Second cohort without prior surgical exploration: ADR - 45 mg/sqm; CACP - 100 mg/sqm. Second cohort with prior surgical exploration: ADR - 40 mg/sqm; CACP - 100 mg/sqm. Third cohort with prior surgical exploration: ADR - 50 mg/sqm; CACP - 100 mg/sqm. All additional patients: ADR - 60 mg/sqm; CACP - 100 mg/sqm. Give all drugs iv (ADR - slow push; CACP - 1 ml/min) q 3 weeks. After one course of therapy, continue until progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 and 25 mg vials; ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 02/80

4.0008 PHASE II SEQUENTIAL CHEMOTHERAPY WITH BLEOMYCIN/MITOMYCIN-C FOR RECURRENT OR METASTATIC SQUAMOUS CELL CARCINOMA OF THE CERVIX

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PROTOCOL NUMBER(S) NCOG-P-5C81

OBJECTIVES:

I. Evaluate the objective response rate, duration of response, and toxicity of the sequential combination of bleomycin and mitomycin-C.

PROTOCOL ENTRY CRITERIA: Patients with measurable disease of recurrent or metastatic squamous cell carcinoma of the cervix, no longer amenable to surgery or radiotherapy. Patients must have adequate hepatic, renal and bone marrow function, a life expectancy of at least 6 weeks or a Karnofsky performance score of less than 50. They must not have had prior therapy with study agents and must have recovered from any previous radiation or chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction and Maintenance: Sequential 2-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Disease site: pelvic, metastatic, or both; prior chemotherapy; prior pelvic radiotherapy; performance status: above 80 vs. below 80.

SPECIAL STUDY PARAMETERS: Liver and bone scan, IVP, lymphangiogram or CT scan.

END POINTS: Response/remission rate, duration of response, length of survival.

CURRENT STATUS: 20 patients will be entered in 10 months.

DOSAGE SCHEDULE:

Induction: BLEO - 5 units iv on days 1 through 7 (maximum cumulative dose 400 units); MITO - 5 mg/sqm iv on day 8. Repeat q 7 days for 3 courses, then evaluate patients. Remove patients with disease progression from study. Give two additional courses to patients with stable disease or partial regression, if complete response after 3 courses or complete or partial response after 5 courses, enter patients to Maintenance.

Maintenance: BLEO/MITO - as in Induction, but repeat course once a month, until maximum dose of BLEO has been given or relapse is noted.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 mg ampules; MITO - 5 mg vials.

DATE SUMMARIZED: 10/78

4.0009 NEUTRON RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX

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PROTOCOL NUMBER(S) RTOG-7608

OBJECTIVES:

I. Assess the absence of persistent or recurrent tumor in the pelvis

II. Determine the length and quality of survival.

III. Assess the incidence of distant metastases and complications of treatment.

PROTOCOL ENTRY CRITERIA: Patients, nonpregnant and without prior therapy, with biopsy proof of Stage III or IV A (FIGO classification) squamous cell carcinoma of the cervix. Patients must not have evidence of paraaortic nodal or distant metastasis, or simultaneous or prior tumor at another site except for controlled skin and lip carcinoma, other than melanoma.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Photons only (x-ray generators capable of producing photon beams with a peak energy of 4 MeV or greater or Cobalt-60). Acceptable SSD is 80 cm or greater.

Arm II: Radiotherapy. Neutrons only (cyclotrons using neutron beams of 21.5 MeV or greater deuteron energy, or 14 MeV D-T neutron generators). The minimum acceptable SSD is 125 cm.

Arm III: Cyclic mixed Radiotherapy. Neutrons (2 fractions/week) and photons (3 fractions/week).

Arm IV: Sequential mixed Radiotherapy. Photons followed by neutrons.

STRATIFICATION BY: Participating institutions, stage of disease, paraaortic nodes on lymphangiograms - negative or equivocal.

SPECIAL STUDY PARAMETERS: Chest X-ray, lymphangiogram, IVP, cystoscopy, proctoscopy.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response, length and quality of survival, regional/distant metastases.

CURRENT STATUS: About 240 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Photon irradiation - 5000 rad total pelvis irradiation in 25 fractions in 5 weeks (4 field-box technique; treat 2 fields per day 5 days/week). Supplemental intracavitary irradiation - sources, radium or cesium or cobalt, 4000 -5000 mg-hrs; plus 600 rads external megavoltage irradiation to the involved pelvic side wall (optional). In absence of intracavitary irradiation, deliver 1000 to 1600 rads in 1 to 2 weeks as supplemental megavoltage boost therapy.

Arm II: Neutron irradiation - 5000 rad eq total pelvis irradiation in 25 to 29 fractions in 5 to 6 weeks treatment field as in Arm I. Rest 4 days/week. Supplemental intracavitary irradiation or boost therapy - same as in Arm I.

Arm III: Combined photon and neutron irradiation - 5000 rad eq in 25 fractions/5 weeks using combined fast neutrons (2 fractions/week) and conventional radiotherapy (3 fractions/week). Supplemental intracavitary irradiation or boost therapy - same as in Arm I.

Arm IV: Photon irradiation - 3000 rad/15 10-17 fractions/3 to 3 1/2 weeks 4 days/week with megavoltage irradiation. Neutron irradiation - 2000 rad eq/8 to 10 fractions/2 to 2 1/2 weeks (4 days/week) following photon irradiation. Supplemental intracavitary irradiation or boost therapy - same as in Arm I.

Follow all patients until death.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/76

PATIENT ACCRUAL: 00440578

4.0010 PHASE I-II STUDY OF MISONIDAZOLE PLUS RADIOTHERAPY FOR STAGE IIIB OR IVA SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX

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PROTOCOL NUMBER(S) RTOG-7906

OBJECTIVES:

I. Determine the tolerance of misonidazole (MNI) in a large group of patients with less advanced carcinoma of the cervix than the experience obtained in the Phase I Study in the RTOG.

II. Determine the tolerance of the unusual radiation fractionation scheme proposed in this protocol in terms of acute and late normal tissue reaction and damage.

III. Observe the relationship between dose of MNI in mg/sqm, mg/kg, and the 4 to 6 hours blood level of misonidazole.

IV. Determine tumor tissue levels of MNI in assessable sites.

V. Establish that the tumor clearance rate, disease-free interval, local tumor control rate and relapse patterns are within the expected ranges for this stage carcinoma of the cervix.

VI. Lay the basis for a subsequent Phase III randomized study of MNI in squamous cell carcinoma of the cervix.

PROTOCOL ENTRY CRITERIA: Patients 18 to 75 years old with histologically proven, measurable FIGO Stage III or IVA squamous cell carcinoma of the uterine cervix. Patients must not have distant metasases; minimum life expectancy must be 12 months and Karnofsky performance status at least 40%. Patients must have had no prior radiotherapy to the tumor volume; they must receive no concurrent chemotherapy. Prior chemotherapy must have terminated 2 weeks prior to entry. Patients must have adequate bone marrow, renal and hepatic function and acceptable neurologic and metabolic status.

PROTOCOL OUTLINE: Nonrandomized study.

Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037; plus Radiotherapy with Cobalt-60 or greater voltage equipment.

STRATIFICATION: Participating institutions, disease stage, histopathologic grade; performance status; prior surgery.

SPECIAL STUDY PARAMETERS: IVP, cystoscopy, sigmoidoscopy.

END POINTS: Toxicity/morbidity of treatment, disease-free interval, relapse rate, response/remission rate.

CURRENT STATUS: 25 patients will be entered in 8 months.

DOSAGE SCHEDULE:

MNI - 1.25 gm/sqm (maximum dose 15 gm) po 4 to 6 hours prior to each Radiotherapy treatment; 4000 rad given over 7 weeks in 10 fractions to the whole pelvis plus brachytherapy - 50 to 100 mg of radium insertion (at least 3000 rad to the central pelvic reference point) or external boost - 2000 rad in 10 fractions to residual tumor areas. Follow up patients at conclusion of Radiotherapy, 6 weeks later and q 2 months for 1 year, then q 3 months for 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 04/79

4.0011 PELVIC VS PELVIC PLUS PARA-AORTIC RADIOTHERAPY IN STAGE IIB OR BULKY IB, IIA CERVICAL CARCINOMA

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PROTOCOL NUMBER(S) RTOG-7920

OBJECTIVES:

I. Determine the value of pelvic radiation vs. pelvic and para-aortic node irradiation when para-aortic nodes are clinically negative in Stage IIB, bulky Stage IB and IIA cervical carcinoma as measured by relapse-free survival and total survival.

II. Determine the increased morbidity, if any, of extended para-aortic irradiation as against pelvic irradiation only in terms of early and late complications.

III. Determine the superiority, if any, of various treatment techniques employed in para-aortic irradiation.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven FIGO Stage IIB or bulky Stage IB/IIA cervical carcinoma (without clinical evidence of para-aortic nodal involvement, April 1980 Revision) who have not undergone curative surgery or prior radiotherapy to the target site. Patients must be between 18 and 75 years old with a Karnofsky performance status of 40 or better. Patients must have adequate bone marrow and renal status.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy with supervoltage equipment (Co-60 or higher energy) to the pelvis.

Arm II: Radiotherapy as in Arm I to the pelvis and para-aortic region.

STRATIFICATION: Participating institutions; histology: squamous cell vs. all others; FIGO Stage: IB, IIA vs. IIB; para-aortic lymph node status: negative vs. unevaluated.

SPECIAL STUDY PARAMETERS: SMA-18; IVP; cytoscopy; sigmoidoscopy; liver, lymph node, and bone scans; retrograde pyelogram; lymphangiogram.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: 364 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: Pelvic Radiotherapy - 4000 to 5000 rad in 4.5 to 6.5 weeks.

Arm II: Pelvic and Para-Aortic Radiotherapy - 4400 to 4500 rad in 4.5 to 5.5 weeks to both regions.

Intracavitary radiation may be used in addition at the discretion of the investigators.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 02/80

4.0012 PHASE III RADIOTHERAPY WITH OR WITHOUT RADIOSENSITIZATION WITH MNI FOR STAGE IIIB AND IVA SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX

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PROTOCOL NUMBER(S) RTOG-8005

OBJECTIVES:

I. Determine the toxicity of daily low-dose misonidazole (MNI) with standard fractionated radiation therapy.

II. Compare the tumor clearance rate, disease-free interval, local tumor control rate, and tumor-relapse patterns associated with radiation therapy alone and radiation therapy plus misonidazole.

PROTOCOL ENTRY CRITERIA: Patients 18 to 75 years of age with histologically proven, measurable squamous cell carcinoma of the uterine cervix of Stages IIIB or IVA (FIGO). The Karnofsky status must be at least 50, and the patient must be able to withstand radiotherapy in terms of bone marrow function, blood counts, and renal and hepatic function. The neurological status must be acceptable, and there must be a reasonable expectation of followup. There must be no prior surgery for cervical cancer, no prior irradiation of the pelvis, and no prior or concurrent chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037; plus megavoltage irradiation (Cobalt-60 range or greater) of the whole pelvis, followed by intracavitary irradiation with Cobalt-60, Radium, or Cesium.

Arm II: Radiotherapy. Whole pelvic irradiation followed by intracavitary irradiation.

STRATIFICATION BY: Performance status, Karnofsky: 50-70 vs. 80-100; para-aortic nodes: positive vs. negative or equivocal; disease stage: IIIB vs. IVA; participating institutions.

SPECIAL STUDY PARAMETERS: IVP; lymphangiogram; cytoscopy; sigmoidoscopy; metastatic evaluation of brain, liver, and bone; misonidazole serum levels.

END POINTS: Response/remission rate, disease-free interval, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 130 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 4600 rads daily in fractions of 180-200 rads to whole pelvis 5 days/week for 4.5 to 5 weeks, plus 1000 rads parametrial boost to 5600 rads, followed by one or two intracavitary brachytherapy insertions (50-85 mg Radium or equivalent) for total of 8000 rads. If brachytherapy insertion is not possible, the patient will receive an external irradiation boost of an additional 2000-2400 rads using a shrinking field technique. If the para-aortic lymph nodes are involved, the region will receive 4500-4600 rads in daily fractions of 160-180 rads 5 days/week for 5 to 5.5 weeks, followed by a boost of 500-600 rads. The treatment may be concurrent with the pelvic irradiation or be given separately. MNI - 400 mg/sqm po daily 5 days/week for 5.5 to 6 weeks (maximum dose 12 g/sqm), given 2 to 4 hours before Radiotherapy.

Arm II: Radiotherapy as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 12/80

4.0013 PHASE II COMBINATION CHEMOTHERAPY WITH CACP VS MITO/CACP VS MITO/VCR/BLEO/CACP FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE CERVIX

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PROTOCOL NUMBER(S) SWOG-7936

OBJECTIVES:

I. Determine the response rate, duration of responses, and survival after treatment with cis-platinum (CACP) vs. CACP/mitomycin-C (MITO) vs. CACP/MITO/vincristine (VCR)/Bleomycin (BLEO) in patients with advanced squamous cell carcinoma of the cervix not amenable to surgery or radiotherapy.

II. Document the nature and extent of the hematologic and nonhematologic side effects of the drug regimens.

PROTOCOL ENTRY CRITERIA: Patients with measurable incurable squamous cell carcinoma of the cervix not amenable to surgery or radiotherapy. Patients must have a minimum life expectancy of 6 weeks, adequate hepatic, renal, and pulmonary function. Patients must have no prior therapy with the study agents, and a Karnofsky performance status of 50 or better.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. Mitomycin-C, MITO, NSC-26980; Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

Arm II: 2-Drug Combination Chemotherapy. MITO; CACP.

Arm III: Single-agent Chemotherapy. CACP.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment, duration of response, duration of survival, relapse rate.

CURRENT STATUS: 75 to 300 patients to be entered.

DOSAGE SCHEDULE:

Arm I: Induction. MITO - 10 mg/sqm iv on days 2 and 44; VCR - 0.5 mg/sqm iv on days 2, 4, 44, and 46; BLEO - 30 mg iv infusion on days 1 through 4 and 43 through 46; CACP - 50 mg/sqm (maximum total dose 400 mg/sqm) iv on days 1, 22, 43, and 64. Enter patients with complete or partial response to Maintenance. Remove all others. Maintenance. MITO - 10 mg/sqm iv on day 86. Repeat course q 6 weeks. CACP - 50 mg/sqm iv on day 86. Repeat course q 3 weeks.

Arm II: Induction. MITO - 12 mg/sqm iv on days 1 and 43; CACP - 50 mg/sqm on days 1, 22, 43, and 64. Enter patients with complete or partial response to Maintenance. Remove all others. Maintenance. MITO, CACP as in Arm I-Maintenance.

Arm III: Induction. CACP - 50 mg/sqm iv on days 1, 22, 43, and 64. Enter patients with complete or partial response to Maintenance. Remove all others. Maintenance. CACP - 50 mg/sqm iv on day 86. Repeat course q 3 weeks.

Follow all patients for survival. Remove patients from study if disease progresses after day 43.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MITO - 5 mg vials; VCR - 1 or 5 mg vials; BLEO - 15 mg vials; CACP - 10 or 50 mg vials.

DATE SUMMARIZED: 02/80

4.0014 BLEO/CTX/ADR/CACP VS BLEO/CACP IN STAGE III-IV CERVICAL CARCINOMA WITH 5-FU/VCR/ADR/MITO OR 5-FU/VCR/MITO AFTER FAILURE

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PROTOCOL NUMBER(S) MAYO-796251; NCCTG-796251

OBJECTIVES:

I. Compare the therapeutic efficacy of bleomycin/cyclophosphamide/adriamycin/cis-platinum with that of bleomycin/cis-platinum using bleomycin in only the first 4 courses in patients with Stage III-IV cervical carcinoma.

II. Evaluate a combination of 5-fluorouracil/vincristine/mitomycin-C for failures on the 4-drug regimen and a combination of 5-fluorouracil/vincristine/adriamycin/mitomycin-C for failures on the 2-drug regimen.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage III or IV cervical carcinoma or advanced carcinoma of vulvar or vaginal origin for which no better treatment is available. The expected survival must be at least 2 months and the ECOG performance status must be 3 or better. Bone marrow, liver, and kidney function must be adequate, and patients must have recovered from recent surgery, radiotherapy, or chemotherapy. Patients may not have received prior chemotherapy with any of the 7 protocol drugs. There must be no significant infection or active heart disease. Patients must be under the age of 75 years and must have adequate pulmonary function.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arm I or II. Enter failures on Arm I to Arm III and failures on Arm II to Arm IV.

Arm I: 4-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875; Bleomycin, BLEO, NSC-125066.

Arm II: 2-Drug Combination Chemotherapy. CACP; BLEO.

Arm III: 3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Vincristine, VCR, NSC-67574; Mitomycin-C, MITO, NSC-26980.

Arm IV: 4-Drug Combination Chemotherapy. 5-FU; VCR; ADR; MITO.

STRATIFICATION BY: Tissue of origin (cervix vs. vulva vs. vagina), histologic grade (1 or 2 vs. 3 or 4), performance status (0 or 1 vs. 2 or 3), measurable disease (yes vs. no), dominant pattern (pelvic disease vs. extrapelvic disease).

SPECIAL STUDY PARAMETERS: Tumor measurements, performance score, hematologic parameters, blood chemistries, chest x-ray.

END POINTS: Response/remission rate, duration of response, objective tumor response.

CURRENT STATUS: About 30 patients per year will be accrued for 3 years.

DOSAGE SCHEDULE:

Arm I: CTX - 400 mg/sqm iv push on day 1; ADR - 40 mg/sqm iv over 5-10 minutes on day 1; CACP - 60 mg/sqm iv over 2 hours with concomitant diuresis on day 1; BLEO - 20 U/sqm/day by continuous iv infusion on days 1, 2, and 3 of the first 4 courses only. Courses to repeat q 4 weeks. Total cumulative ADR dose limited to 520 mg/sqm. Total cumulative BLEO dose limited to 240 U/sqm with an absolute maximum of 400 U. Stable or improved patients continue until progression; those with progressive disease enter Arm III.

Arm II: CACP - 60 mg/sqm iv over 2 hours with concomitant diuresis on day 1; BLEO - 20 U/sqm/day by continuous iv infusion on days 1, 2, and 3 for first 4 courses. Repeat courses q 3 weeks. BLEO dose limitation as in Arm I. Stable and improved patients continue until progression; those with progressive disease enter Arm IV.

Arm III: 5-FU - 600 mg/sqm iv push on days 1, 8, 29, and 36; VCR - 1.2 mg/sqm (maximum 2 mg) iv push on days 1, 8, 29, and 36; MITO - 12 mg/sqm iv push on day 1. Repeat courses q 8 weeks.

Arm IV: 5-FU - 600 mg/sqm iv push on days 1, 8, 29, and 36; VCR - 1.2 mg/sqm (maximum 2 mg) iv push on days 1, 8, 29, and 36; ADR - 30 mg/sqm iv push on days 1 and 29; MITO - 10 mg/sqm iv push on day 1. Repeat courses q 8 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 U ampules; CTX - 100, 200, and 500 mg vials; ADR - 10 mg vials; CACP - 10 mg vials; 5-FU - 500 mg ampules; MITO - 5 mg vials; VCR - 1 and 5 mg ampules.

DATE SUMMARIZED: 07/80

4.0015 C. PARVUM IMMUNOTHERAPY, CHEMOTHERAPY WITH ADR AND RADIOTHERAPY FOR SQUAMOUS CARCINOMA OF THE CERVIX

Wharton, J. T., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-29

OBJECTIVES:

I. Determine whether C. parvum augments the therapeutic effectiveness of irradiation therapy or chemotherapy for squamous carcinoma of the cervix.

II. Determine whether treatment with C. parvum induces change in the immunocompetence of patients, and if this occurs, whether it correlates wiith the prognosis.

PROTOCOL ENTRY CRITERIA: Patients with Stages IIB, III and IV squamous carcinoma of the cervix. Patients to be treated iv with C. parvum immunotherapy must be less than 60 years old and must not have underlying cardiovascular or pulmonary disease.

PROTOCOL OUTLINE:

Part I: Randomized study. Enter patients with positive nodes resected at laparotomy.

Arm I: Radiotherapy. Extended field irradiation.

Arm II: Radiotherapy plus Immunotherapy. Corynebacterium parvum, C. parvum.

Part II: Randomized study. Enter patients with non-resectable lymph node metastases.

Arm III: Radiotherapy plus Single-agent Chemotherapy. Radiotherapy as in Arm I. Chemotherapy: Adriamycin, ADR, NSC-123127 plus unspecified Maintenance Chemotherapy.

Arm IV: Radiotherapy plus Immunotherapy plus Chemotherapy. Arm III Radiotherapy plus Chemotherapy plus Arm II Immunotherapy with C. parvum.

STRATIFICATION BY: Participating institutions, extent of disease.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, disease-free interval, survival rate.

CURRENT STATUS: About 30 patients will be entered per year.

DOSAGE SCHEDULE:

Part I:

Arm I: Following laparotomy - time interval not specified - enter patients to extended field radiotherapy: 1. Administer to patients with nodes confined to the obturator hypogastric complex radiotherapy through the standard 15 by 15 cm parallel opposing fields. 2. Administer to patients with metastatic cancer in external iliac, common iliac, or aortic node areas 850 rads/week for a total of 4500 rads with a 25 MEV linear accelerator. If necessary, administer an additional 1000 rads to the pelvis through a 15 by 15 opposing portal. 3. Administer intracavitary radium to patients who have adequate anatomy. 4. Administer additional external radiotherapy through a smaller portal to patients with poor anatomy. 5. Administer to patients with very bulky central tumors supplemental fast-neutron therapy in addition to 4500 rads given with the linear accelerator as in 2.

Arm II: C. parvum - 5 mg/sqm iv given over 2 hours beginning 14 days following laparotomy. Repeat course after 7 days. Begin radiotherapy as in Arm I 2-3 days before 2nd course of C. parvum on days 12 and 22, and thereafter q 45 days.

Part II:

Arm III: Radiotherapy, as in Arm I. One month following completion of radiotherapy begin: ADR - 60 mg/sqm on day 1 and day 22. Repeat course q 21 days until the total maximum cumulative dose of 450 mg/sqm has been given. Then give Maintenance Chemotherapy (type not specified) for a total of 1 year of chemotherapy.

Arm IV: Radiotherapy and Chemotherapy as in Arm III. Immunotherapy as in Arm II.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/76

4.0016 SEQUENTIAL CHEMOTHERAPY WITH CTX, HMM, ADR FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE CERVIX

Wharton, J. T., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-30

OBJECTIVES:

I. Evaluate the objective tumor response, duration of response, relative toxicity and effect on the patients' performance status of three chemotherapeutic drugs.

II. Determine which of these drugs and drug sequences achieve the best overall results by analysis of survival data.

PROTOCOL ENTRY CRITERIA: Patients previously untreated by chemotherapy who have recurrent or metastatic squamous carcinoma of the cervix not potentially curable by surgery or radiotherapy. Patients must have adequate bone marrow reserves and must be eligible for all arms of the study.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm II: Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

Arm III: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Sequential cross-over if disease persists or drug tolerance is reached.

STRATIFICATION BY: Measurability of disease parameters.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Objective tumor response, response/remission rate, response duration, toxicity/morbidity of treatment, survival rate, quality of response.

CURRENT STATUS: About 75 patients will be entered per year.

DOSAGE SCHEDULE:

Arm I: CTX - 8 mg/kg/day iv on days 1 through 5 q 28 days.

Arm II: HMM - 8 mg/kg/day po continuously if wbc remains above 3000 and platelet count above 100,000.

Arm III: ADR - 80 mg/sqm (total maximal cumulative dose 480 mg) iv single dose q 28 days.

Evaluate patients after 8 weeks of therapy. If disease is progressing or tolerance of initial drug has been reached, rest patient 4 weeks then cross over to alternate arm.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/77

4.0017 LARGE DOSE/FRACTION RADIOTHERAPY AND HYPOXIC CELL SENSITIZER MISONIDAZOLE FOR ADVANCED CARCINOMA OF THE UTERINE CERVIX

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PROTOCOL NUMBER(S) MDAR-315; MDA-RT8/rt60

OBJECTIVES:

I. Increase palliative effect, local control of disease, and rate of survival in patients with advanced cervical carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with advanced uterine cancer with massive disease in the pelvis, who are not candidates for conventional radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy.

Arm II: Radiotherapy plus Hypoxic Cell Sensitization. Misonidazole, MNI, NSC-261037.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, survival rate, palliation, objective tumor response.

CURRENT STATUS: 10 to 15 patients per year will be entered.

DOSAGE SCHEDULE:

Arm I: 1000 rad tumor dose in one fraction using parallel opposed anterior and posterior fields to the pelvis q month for a total of 3 courses if the clinical situation permits.

Arm II: MNI - 4 g/sqm (route not given) 4 to 5 hours prior to radiation. Radiotherapy, as in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/79

4.0018 BLEOMYCIN/MITOMYCIN-C INDUCTION AND CYCLOPHOSPHAMIDE MAINTENANCE FOR RECURRENT SQUAMOUS CELL CARCINOMA OF THE CERVIX

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PROTOCOL NUMBER(S) MDAR-340; MDA-G/gyn12

OBJECTIVES:

I. Evaluate the combination of bleomycin and mitomycin-C in patients with recurrent and/or distant metastatic squamous cell carcinoma of the cervix not amenable to surgery or irradiation.

II. Determine the toxicity of this regimen.

PROTOCOL ENTRY CRITERIA: Patients previously untreated by chemotherapy with histologically proven distant metastatic or locally recurrent squamous cell carcinoma of the cervix not amenable to surgery or radiotherapy. Patients must have adequate pulmonary and hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 2-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; Mitomycin-C, MITO, NSC-26980.

Maintenance: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Functional vital capacity, creatinine clearance.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 30 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Induction: BLEO - 5 mg iv on days 1 through 7; MITO - 7 mg/sqm iv on day 8. Rest 7 days, then repeat therapy for a total of 5 courses if toxicity permits.

Maintenance: Begin 6 weeks after the last dose of MITO. CTX - 1500 mg/sqm iv on day 1 q 4 weeks if hematologic toxicity permits.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/79

4.0019 COMBINATION CHEMOTHERAPY WITH CACP/ARA-C FOR SQUAMOUS CERVICAL CARCINOMA

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PROTOCOL NUMBER(S) MDAR-409; MDA-G-8001

OBJECTIVES:

I. Determine the maximum tolerated dose of the combination of cis-platinum and cytosine arabinoside administered intravenously.

II. Evaluate the response rate of these drugs in patients with persistent or recurrent squamous cervical carcinoma, once the maximum tolerated dose of the combination is obtained.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, recurrent or persistent, nonoperable squamous carcinoma of the cervix. Easily measurable lesions are desirable. Patients must have a life expectancy of at least 60 days and have adequate bone marrow, liver, and renal function. Patients must have received no previous intensive chemotherapy and must have been off all previous chemotherapy or radiotherapy for at least 4 weeks at the time of entry. Patients must have recovered from any resultant toxic effects.

PROTOCOL OUTLINE: Nonrandomized study. Patients who reach tolerance dose or show progression prior to tolerance dose enter Maintenance.

2-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Cytosine arabinoside, ARA-C, NSC-63878.

Maintenance and Alternative Treatment:

Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Granulocyte and platelet counts, renal and hepatic function tests.

END POINTS: Response/remission rate, disease-free interval, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: The annual accrual of 20 easily evaluable patients is estimated. Study can be completed in 15 months.

DOSAGE SCHEDULE:

CACP - 75 mg/sqm iv (total cumulative dose is 400 mg/sqm); ARA-C - 500 mg/sqm iv, with 2 incremental doses at 750 mg/sqm and 1000 mg/sqm. Courses are repeated q 3-4 weeks provided no significant toxicity is present. At least 3 patients will be studied at each dose level and evaluated for at least 2 weeks before additional patients are started on the next escalated dose level. Each patient is treated at one dosage level only.

Maintenance:

Pulse CTX - 1500 mg iv.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

4.0020 CHEMOTHERAPY WITH BLEOMYCIN/CIS-PLATINUM FOR ADVANCED CERVICAL CANCER

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PROTOCOL NUMBER(S) MSKCC-7977

OBJECTIVES:

I. Improve the response rate of patients with cervical cancer who are not candidates for surgery or radiotherapy by combination chemotherapy with bleomycin/cis-platinum.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable cervical cancer who are not candidates for curative surgery or radiotherapy. Patients must have adequate kidney function, at least 75% normal pulmonary function, a performance status above 50, and an expected survival greater than 2 months. Patients must not have had prior chemotherapy or have a clinical hearing deficit.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; cis-Platium, CACP, NSC-119875.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: CEA; 5-prime nucleotidase; bone, liver and brain scan; audiogram and CAT scan if indicated.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

BLEO - 10 U/sqm (maximum total dose 400 U/sqm) iv 24 hour infusion for 7 days; CACP - 120 mg/sqm iv with hydration and mannitol diuresis on day 1. Repeat course q 4 weeks.

Dosage modifications for toxicity are given.

DATE SUMMARIZED: 11/79

4.0021 SURGERY PLUS ADJUVANT CHEMOTHERAPY WITH CACP/MITO/BLEO PLUS RADIOTHERAPY FOR CERVICAL CANCER WITH PARA-AORTIC LYMPH NODE DISEASE

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PROTOCOL NUMBER(S) NCI-80-C-145; NCI-MB-140

OBJECTIVES:

I. Determine whether chemotherapy with cis-platinum/mitomycin-C/bleomycin plus radiotherapy can prolong the overall survival of F.I.G.O. Stage IB-IIIB cervical cancer patients who have undergone para-aortic lymph node dissection.

II. Determine whether the in vitro colony-forming assay of cervical cancer stem cells can predict the results of this adjuvant chemotherapy.

III. Determine the accuracy of lymphangiograms and lymph node aspiration in determining the status of the para-aortic nodes.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven cervical cancer, F.I.G.O. clinical Stage IB-IIIB, with para-aortic lymph node involvement (defined as nodes between the renal vessels and bifurcation of the aorta) verified by biopsy. Patients must be less than 70 years of age; there must be adequate hematologic, renal and hepatic function. There must be no history of prior malignancy other than skin cancer (exclusive of malignant melanoma). Patients must have received no prior radiotherapy or chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Surgery plus 3-Drug Combination Chemotherapy plus Radiotherapy. Para-aortic lymph node dissection; followed by cis-Platinum, CACP, NSC-119875; Mitomycin-C, MITO, NSC-26980; Bleomycin, BLEO, NSC-125066; plus whole pelvis irradiation.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; pelvic exam; x-ray studies and scans; sigmoidoscopy; cystoscopy; pulmonary function tests; lymph node aspirate; audiogram.

END POINTS: Disease-free interval, survival.

CURRENT STATUS: Approximately 25 patients will be entered onto this study.

DOSAGE SCHEDULE:

Not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

4.0022 RADIOTHERAPY VS RADIOTHERAPY PLUS ADJUVANT IMMUNOTHERAPY WITH C. PARVUM FOR STAGE II CARCINOMA OF THE UTERINE CERVIX

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Aires, Argentina

PROTOCOL NUMBER(S) ARG-RNH-101

OBJECTIVES:

I. Compare the disease-free period and survival of patients with stage II epidermoid carcinoma of the uterine cervix, treated with radiotherapy vs. radiotherapy plus C. parvum immunotherapy.

II. Evaluate C. parvum immunotherapy efficiency as an adjuvant to radiotherapy and the combined modality toxicity.

III. Determine if C. parvum alters the tissue acceptance to that type of treatment.

PROTOCOL ENTRY CRITERIA: Patients under 75 years old with measurable, histologically confirmed U.I.C.C. stage II carcinoma of the uterine cervix. Patients must have a minimum life expectancy of 3 months, a Karnofsky performance status better than 50 and adequate hematologic, renal and hepatic function. Patients must not have had prior therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy.

Arm II: Radiotherapy plus Immunotherapy. Corynebacterium parvum, Burroughs Wellcome, C. parvum, B.W., NCS-220537.

STRATIFICATION: Age: 20 to 40 vs. 40 to 60 vs. over 60; disease stage: IIA vs. IIB.

SPECIAL STUDY PARAMETERS: Excretory urography; cystoscopy; rectoscopy; immunologic status including rosette tests.

END POINTS: Response/remission rate; disease-free interval, survival rate, toxicity/morbidity of treatment, survival time, objective tumor response.

CURRENT STATUS: 40 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 8000 rad in 2 doses by intracavitary cesium followed by 5000 rad in 25 days to each parametrium (therapy may begin with total pelvic Co-60 radiation - 4000 rad in 20 days followed by 6000 rad intracavitary cesium and 1500 rad in 8 days to the parametrium.)

Arm II: Radiotherapy, as in Arm I. C. parvum - 0.25 mg/sqm iv on day 1, 0.50 mg/sqm on day 3, 0.75 mg/sqm on day 5, 1 mg/sqm on day 7, then 2 mg/sqm iv q 7 days for 4 weeks, followed by 4 mg/sqm iv q 15 days for 2 years or as long as disease progression is apparent.

Dosage modifications for toxicity are given.

DOSAGE FORMS: C. parvum - 2 mg ampules.

DATE SUMMARIZED: 11/79

4.0023 RADIOTHERAPY VS RADIOTHERAPY PLUS ADJUVANT IMMUNOTHERAPY WITH C. PARVUM FOR STAGE III CARCINOMA OF THE UTERINE CERVIX

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Aires, Argentina

PROTOCOL NUMBER(S) ARG-RNH-102

OBJECTIVES:

I. Compare the disease-free period and survival of patients with stage II epidermoid carcinoma of the uterine cervix, treated with radiotherapy vs. radiotherapy pluc C. parvum immunotherapy.

II. Evaluate C. parvum immunotherapy efficiency as an adjuvant to radiotherapy and the combined modality toxicity.

III. Determine if C. parvum alters the tissue acceptance to that type of treatment.

PROTOCOL ENTRY CRITERIA: Patients under 75 years old with measurable, histologically confirmed U.I.C.C. stage III carcinoma of the uterine cervix. Patients must have a minimum life expectancy of 3 months, a Karnofsky performance status better than 50 and adequate hematologic, renal, and hepatic function. Patients must not have had prior therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Cobalt-60; intracavitary Cesium.

Arm II: Radiotherapy plus Immunotherapy. Corynebacterium parvum; Burroughs-Wellcome; C. parvum; B.W.; NSC-220537.

STRATIFICATION: Age: 20 to 40 vs. 40 to 60 vs. over 60; disease stage: IIIA vs. IIIB.

SPECIAL STUDY PARAMETERS: Excretory urography, rectoscopy, immunologic status including rosette tests, proteinogram.

END POINTS: Response/remission rate, disease-free interval, survival rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 60 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 4000 rad over 20 days followed by 6000 rad of intracavitary Cesium followed by 5000 rad Co-60 Radiotherapy to both parametria in 25 days with central protection of the pelvis.

Arm II: Radiotherapy as in Arm I; C. parvum - 0.25 mg/sqm iv on day 1; 0.5 mg/sqm on day 3; 0.75 mg/sqm on day 5; 1 mg/sqm on day 7, then 2 mg/sqm q 7 days for 4 weeks, followed by 4 mg/sqm q 15 days for 2 years or as long as disease progression is apparent.

Dosage modifications for toxicity are given.

DOSAGE FORMS: C. parvum - 2 mg ampules.

DATE SUMMARIZED: 11/79

4B. OVARY

4.0024 CACP/ADR/HMM ALTERNATING WITH CACP/ADR/HMM/C. PARVUM FOR STAGE III AND IV OVARIAN CANCER

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53715, United States of America

PROTOCOL NUMBER(S) EST-PA-879

OBJECTIVES:

I. Determine the feasibility of repeated intraperitoneal administration of C. parvum in association with a combination drug therapy with cis-platinum (CACP), hexamethylmelamine (HMM), and adriamycin (ADR) in patients with Stage III and IV ovarian cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage III or IV ovarian cancer. Patients must have had no prior therapy with CACP, HMM, or C. parvum. Patients must have adequate renal, hematologic, and cardiac function, and no significant high-frequency hearing loss.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy alternating with Single-agent Intraperitoneal (ip) Immunotherapy. cis-Platinum, CACP, NSC-119875; Adriamycin, ADR, NSC-123127; Hexamethylmelamine, HMM, NSC-13875; plus Corynebacterium parvum, C. parvum, NSC-220357.

STRATIFICATION BY: Participating institutions; tumor burden: operable (optimal vs. suboptimal) vs. inoperable.

SPECIAL STUDY PARAMETERS: Liver function tests; skin tests; CEA; IVP; audiogram; immunoglobulin levels; humoral immunity; Gallium scan; abdominal CT scan.

END POINTS: Toxicity/morbidity of treatment; response/remisson rate.

CURRENT STATUS: 20 to 30 patients will be entered.

DOSAGE SCHEDULE:

Enter all patients 2 to 3 weeks following maximum cytoreductive surgery.

Course 1: Give Furosemide - 40 mg - at the start of a 2-hour saline iv infusion (8 hours for patients intolerant to a brisk fluid load) followed by Mannitol - 12.5 q iv bolus, followed immediately by CACP - 50 mg/sqm iv preceded by ADR - 30 mg/sqm iv (total cumulative dose 550 mg/sqm) - all on day 1; continue Mannitol diuresis with 12.5 g/hour for 6 hours; HMM - 200 mg/sqm po on days 2 through 15.

Course 2: Begin on day 28. Furosemide and Mannitol diuresis; ADR; CACP; as in Course 1; HMM - 200 mg/sqm po on days 2, 3, 4, and 5; C. parvum - 10 mg/sqm ip on day 14. Alternate Courses 1 and 2 and continue therapy until definite relapse or progression, or for 1 year, or indefinitely for patients with a definite response. Institute second-look procedures for patients with complete response in 2 years.

DOSAGE FORMS: ADR - 10 and 50 mg vials; HMM - 50 and 100 mg capsules; CACP - 10 and 25 mg vials; C. parvum - 7 mg ampules.

DATE SUMMARIZED: 06/79

4.0025 PILOT CHEMOTHERAPY WITH CHAD (CTX/HMM/ADR/CACP) PLUS RADIOTHERAPY FOR NON-RESPONDERS WITH ADVANCED OVARIAN CANCER

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PROTOCOL NUMBER(S) EST-PF-878

OBJECTIVES:

I. Determine what percent of patients will be free of ovarian cancer at 6 months following combination chemotherapy with CHAD (CTX/ADR/HMM/CACP) and whether patients with pathologic confirmation of complete remission at this time are cured.

II. Determine tolerance to therapy and therapeutic efficacy of cyclic chemotherapy with monthly whole abdominal irradiation in patients with residual disease after debulking surgery and 6 months of CHAD chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with measurable, evaluable, or non-evaluable histologically diagnosed Stage III or IV epithelial ovarian carcinoma or with unresectable local disease in the pelvis. Patients must not have had prior chemotherapy nor abdominal or pelvic irradiation. Patients must have adequate cardiac, liver, kidney and hematologic functions and an ECOG performance status better than 4.

PROTOCOL OUTLINE: Nonrandomized study, following maximal debulking surgery.

Regimen A. 4-Drug Combination Chemotherapy. CHAD: Cyclophosphamide, CTX, NSC-26271; Hexamethylmelamine, HMM, NSC-13875; Adriamycin, ADR, NSC-123127; Cis-Platinum, CACP, NSC-119875. Perform laparotomy, further debulking surgery if indicated and enter partial responders (PR) with recurrent disease to Regimen B.

Regimen B. 3-Drug Combination Chemotherapy plus Radiotherapy followed by 4-Drug Combination Chemotherapy. CTX; HMM; CACP plus radiation with megavoltage equipment, followed by CHAD, as in Regimen A.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Abdominal ultrasonography, CEA, Audiogram.

END POINTS: Response/remission rate; duration of response; disease-free interval; toxicity/morbidity of treatment; objective tumor response; clinical status at 14 months, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A.

CHAD: CTX - 600 mg/sqm iv on day 1; HMM - 150 mg/sqm po in 3 divided doses after meals on days 8 through 21; ADR - 25 mg/sqm iv on day 1; CACP - 50 mg/sqm iv on day 1 plus hydration and diuresis with Furosemide and Mannitol. Repeat therapy q 28 days for 6 courses. Perform second laparotomy and biopsy previously involved tumor sites. Remove from study patients with stable disease (without response to chemotherapy) or patients with recurrent tumor at laparotomy. Discontinue chemotherapy for patients with no microscopic evidence of disease, follow up until relapse, then remove patients from study. Enter patients with residual disease smaller than that at initial laparotomy or patients with gross residual tumor to Regimen B after further tumor reductive surgery.

Regimen B.

CHD-R: CTX - as in Regimen A, on day 4; HMM - as in Regimen A, on days 11 through 24; CACP - as in Regimen A, on day 4. Administer Radiotherapy - 150 rads to whole abdomen on days 1, 2 and 3. Repeat course q 28 days for 5 courses followed by 3 courses of CHAD, as in Regimen A. Observe CR or PR at end of treatment for duration of remission to time to relapse or progression and survival. Remove patients with progressive disease at anytime from study.

DOSAGE FORMS: HMM - 50 and 100 mg capsules; CACP - 10 and 25 mg vials; ADR - 10 and 50 mg vials; CTX - 100, 200 and 500 mg vials.

DATE SUMMARIZED: 10/79

4.0026 PHASE III CHEMOTHERAPY WITH HIGH AND LOW DOSE CACP PLUS HMM FOR ADVANCED OVARIAN ADENOCARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-2879

OBJECTIVES:

I. Determine effect of high and low dose cis-platinum (CACP)/hexamethylmelamine (HMM) for advanced ovarian adenocarcinoma resistant to alkylating agents.

II. Determine whether pyridoxine reduces neurological toxicity of HMM in this combination.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable or evaluable, Stage III or IV (or unresectable in the pelvis) adenocarcinoma of the ovary (serous, mucinous, undifferentiated, endometrial, clear cell) that has progressed following therapy that included alkylating agents. Patients must have adequate kidney and hematologic function and performance status of 0-3. Patients must not have congestive heart failure, complete intestinal obstruction or prior whole abdominal irradiation.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Hexamethylmelamine, HMM, NSC-13875.

Arm II: 3-Drug Combination Chemotherapy. CACP; HMM; Pyridoxine, NSC-36225.

STRATIFICATION BY: Participating institutions; performance status: 0 or 1 vs. 2 or 3; time from initial diagnosis to entry: up to 12 months vs. more than 12 months.

SPECIAL STUDY PARAMETERS: Liver and kidney function, tumor measurement, audiogram.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 175 patients will be entered in 2.5 years.

DOSAGE SCHEDULE: Randomize patients to Arms IA, IB, IIA, and IIB.

Arm I: CACP - 37.5(A) or 75(B)mg/sqm iv push with 2 hour prior hydration plus Furosemide and Mannitol diuresis on day 1; HMM - 200 mg/sqm po in divided doses immediately after meals on days 8 through 21.

Arm II: CACP - 37.5(A) or 75(B)mg/sqm iv as in Arm I on day 1; HMM - as in Arm I; Pyridoxine - 300 mg po in 3 divided doses on days 1 through 21.

Repeat q 21 days.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; HMM - 50 and 100 mg capsules; Pyridoxine - 50 mg tablets.

DATE SUMMARIZED: 02/80

4.0027 PHASE II ADJUNCTIVE CHEMOTHERAPY WITH L-PAM PLUS IMMUNOTHERAPY WITH C. PARVUM FOR STAGE III EPITHELIAL CARCINOMA OF THE OVARY

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) GOG-25

OBJECTIVES:

I. Compare chemotherapy with melphalan (L-PAM) alone with multimodality therapy with L-PAM plus immunotherapy with C. parvum as adjunctive therapy to surgery for stage III (optimal) epithelial carcinoma of the ovary. Optimal is defined as residual tumor mass no greater than 3 cm at surgery.

PROTOCOL ENTRY CRITERIA: Patients with stage III (optimal) epithelial carcinoma of the ovary. Laparotomy must be performed and a maximum possible amount of tumor excised prior to entry. Total abdominal hysterectomy, salpingo-oophorectomy and omentectomy should be performed when technically feasible. Protocol treatment must begin within 8 weeks of surgery.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm II: Single-agent Chemotherapy and Immunotherapy. L-PAM; Corynebacterium parvum, C. parvum, NSC-220537.

STRATIFICATION BY: Participating institution.

SPECIAL STUDY PARAMETERS: IVP, peritoneal fluid cytology, skin test antigens, FBS.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, disease-free interval, performance status.

CURRENT STATUS: 360 patients are to be entered.

DOSAGE SCHEDULE:

Courses of therapy given only if granulocyte count is greater than 1500 and platelet count is greater than 100,000.

Arm I: L-PAM - 7 mg/sqm po (80 mg maximum dose/course) on days 1 through 5 and q 28 days.

Arm II: L-PAM - as in Arm I. C. Parvum - 4 mg/sqm iv on day 7 and q 28 days.

Patients will receive a minimum of 3 courses. Responders will receive a minimum of 10 courses or 18 months of therapy, whichever comes first. Monitor wbc and platelets once a week and skin test antigens q 3 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-PAM - 2 mg tablets; C. parvum - 0.5 cc ampules.

DATE SUMMARIZED: 01/77

PATIENT ACCRUAL: 00980179

4.0028 PHASE III POSTOPERATIVE CHEMOTHERAPY WITH ADRIAMYCIN FOR PRIMARY OR RECURRENT OVARIAN SARCOMA

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PROTOCOL NUMBER(S) GOG-50

OBJECTIVES:

I. Evaluate the efficacy of adriamycin in the treatment of primary ovarian sarcoma, primary or recurrent, through historic controls.

II. Accumulate additional surgical-pathological data relative to ovarian sarcoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed primary Stage I-IV or recurrent ovarian sarcoma. Patients may have measurable disease, non-measurable disease, or no residual disease postoperatively. Patients must not have tumors considered to be low grade malignancies or reticuloendothelial in origin. Patients must be under 75 years of age; they must have an expected survival of at least one month, and have adequate hematologic, renal, hepatic, and cardiac function. GOG performance status must be better than 4. Patients must have received no previous chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study. All patients undergo initial laparotomy, if indicated.

Regimen A: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Following therapy in Regimen A, patients with CR and those with detectable disease thought to be resectable proceed to Regimen B.

Regimen B: Second-look Surgery.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic, renal, and hepatic function tests; EKG; appropriate radiography; pelvic findings.

END POINTS: Response/remission rate, recurrence rate, objective tumor response, performance status.

CURRENT STATUS: Anticipated annual accrual is 5-8 patients.

DOSAGE SCHEDULE:

Chemotherapy is initiated as soon as the acute effects of Surgery (laparotomy) have resolved.

Regimen A: ADR - 75 mg/sqm bolus or iv infusion q 3 weeks until a maximum cumulative dose of 550 mg/sqm. Patients who develop progressive disease or disqualifying adverse effects go off study at that time. After administration of total cumulative dose, patients with CR or resectable detectable disease are entered into Regimen B.

Regimen B: Second-look Surgery. Patients with no residual disease at second look receive no further therapy until progression; those with residual disease are candidates for GOG Protocol 26.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 09/80

4.0029 PHASE III MELPHALAN CHEMOTHERAPY VS INTRAPERITONEAL RADIOACTIVE CHROMIC PHOSPHATE FOR STAGE I EPITHELIAL OVARIAN CANCER

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PROTOCOL NUMBER(S) GOG-7862; GOG-46

OBJECTIVES:

I. Evaluate the relative effectiveness of Melphalan (L-PAM) vs. intraperitoneal (ip) radioactive chromic phosphate (P-32) as adjuvant therapy in Stage I exclusive of Stage IA (i) G1 and Stage IB (i) G1 epithelial cancers of the ovary.

PROTOCOL ENTRY CRITERIA: Patients with surgical Stage IA (i) G2, G3; IA (ii); IB (i) G2, G3; IB (ii) and IC epithelial cancer of the ovary optimally staged as described in GOG protocol. Patients must have had no prior or concomitant malignancy of any other site except of skin, excluding melanoma. Patients must have had no prior pelvic or abdominal irradiation and/or chemotherapy.

PROTOCOL OUTLINE: Randomized study, following surgery.

Arm I: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm II: Single-agent Radioisotope Therapy. Intraperitoneal radioactive colloidal chromic phosphate, P-32.

STRATIFICATION BY: Disease stage: IA (i) Grade 2, 3; IA (ii) Grade 1, 2 or 3; IB (i) Grade 2, 3 vs. IB (ii) or IC Grade 1, 2, or 3.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, disease-free interval, length of survival, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 93 to 125 patients will be entered in 2 to 3 years.

DOSAGE SCHEDULE:

Begin all therapy within 6 weeks of surgery: TAH/BSO and partial omentectomy.

Arm I: L-PAM - 7 mg/sqm (maximum dose/course 80 mg) po on days 1 through 5 for 4 weeks. Continue for 10 courses or 18 months in responders without evidence of recurrence.

Arm II: Chromic phosphate P-32 - 15 millicuries ip as a single dose following 250 ml normal saline and followed by 500 ml saline. Follow up all patients q 3 months for 2 years, then q 6 months for 3 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/79

4.0030 PHASE II ADJUVANT CHEMOTHERAPY WITH VAC (VCR/ACT-D/CTX) FOR MAXIMALLY RESECTED GERM CELL TUMORS OF THE OVARY

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PROTOCOL NUMBER(S) GOG-7863; GOG-44

OBJECTIVES:

I. Evaluate the effect of prophylactic VAC - vincristine (VCR)/actinomycin-D (ACT-D)/cyclophosphamide (CTX) - in patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (Grades 2 and 3), choriocarcinoma, and malignant mixed germ cell tumors of the ovary, Stage I and II after total removal of all gross tumor.

II. Evaluate the role of serum markers, especially alpha-fetoprotein (AFP) and human chorionic gonadotropin (beta HCG), when these are present, in predicting response and relapse.

III. Determine the role of restaging laparotomy in determining response, predicting outcome, and planning further therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage I or II germ cell tumor of the ovary after complete resection as the primary therapy, or grade 2 or 3 immature teratoma. Patients may have early Stage III disease if all gross tumor is resected. Patients must have adequate bone marrow, renal and hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. VAC: Vincristine, VCR, NSC-67574; Actinomycin-D, ACT-D, NSC-3053; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum alpha-fetoprotein, Beta HCG, IVP, urinary gonadotropins, estrogens, and testosterone.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival time, objective tumor response.

CURRENT STATUS: 30 to 39 patients will be entered in 2 1/2 to 3 years.

DOSAGE SCHEDULE:

Enter patients within 4 to 6 weeks following surgery. ACT-D - 350 micrograms/sqm iv on days 1 through 5; CTX - 150 mg/sqm iv on days 1 through 5; VCR - 1.5 mg/sqm (maximum dose 2 mg) iv on days 1 and 14. Repeat course q 4 weeks for 6 courses. Remove patients with progressive disease from study. Give 3 additional courses to patients with no evidence of disease after restaging laparotomy. Enter patients failing therapy to SWOG-7864.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CTX - 100, 200, and 500 mg vials; ACT-D - 0.5 mg vials.

DATE SUMMARIZED: 02/79

4.0031 PHASE III CHEMOTHERAPY WITH VBP (VBL/BLEO/CACP) AND VAC (VCR/ACT-D/CTX) FOR RECURRENT MALIGNANT GERM CELL TUMORS OF THE OVARY

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) GOG-7864; GOG-45

OBJECTIVES:

I. Evaluate the effect of 4 cycles of VBP: vinblastine (VBL)/bleomycin (BLEO)/cis-platinum (CACP) - in the management of patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (all grades), choriocarcinoma, and malignant mixed germ cell tumors of the ovary with advanced or recurrent disease, incompletely resected.

II. Evaluate the role of serum markers, especially alpha-fetoprotein (AFP) and human chorionic gonadotropin (beta HCG), when these are present, in predicting response and relapse.

III. Evaluate and compare the effect of VAC: vincristine (VCR)/actinomycin-D (ARA-C)/cyclophosphamide (CTX) - in patients found to have persistent disease at the time of restaging laparotomy.

IV. Determine the need for maintenance VBL therapy in patients found free of disease at restaging laparotomy.

PROTOCOL ENTRY CRITERIA: Patients under age 60 with histologically confirmed, incompletely resected Stage II, III, or IV or recurrent malignant germ cell tumors of the ovary. Patients must have adequate hematologic, renal, hepatic, and pulmonary status. Patients must not have had prior therapy with VBL, BLEO, or CACP, but may have failed prior therapy with VAC.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A:

Induction: Enter all patients following total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and maximal removal of bulk tumor. 3-Drug Combination Chemotherapy. VBP: Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875. Enter patients with no evidence of disease to Maintenance, all others with no prior VAC therapy to Regimen B.

Maintenance: Single-agent Chemotherapy. VBL.

Regimen B: 3-Drug Combination Chemotherapy. VAC: Vincristine, VCR, NSC-67574; Actinomycin-D, ACT-D, NSC-3053; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum alpha-fetoprotein and beta HCG, IVP, liver and bone scans, gonadotropin, estrogen and testosterone levels.

END POINTS: Objective tumor response, progression-free interval, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: 30 to 40 patients will be entered in 3.5 years.

DOSAGE SCHEDULE:

Regimen A:

Induction: VBP: VBL - 12 mg/sqm (9 mg/sqm for patients with prior pelvic Radiotherapy) iv on day 1; BLEO - 20 U/sqm (10 U/sqm for patients 13 years old or under; maximum cumulative dose 360 U; maximum single dose 30 U) iv on days 1, 7, and 14 (6 hours after VBL where possible); CACP - 20 mg/sqm iv on days 1 through 5. Repeat course q 3 weeks for 4 courses. Enter patients with progressive disease to Regimen B. Perform restaging laparotomy in all complete responders or patients with partial, apparently resectable response within 6 weeks after the 3rd or 4th course of VBP. If no evidence of disease, enter patients to Maintenance. Enter patients with persistent disease to Regimen B, unless patient had a prior failure on VAC.

Maintenance: VBL - 9 mg/sqm iv on day 1. Repeat course q 4 weeks for 18 months.

Regimen B: VAC: VCR - 1.5 mg/sqm (maximum dose 2 mg) iv on days 1 and 14; ACT-D - 0.35 mg/sqm iv on days 1 through 5; CTX - 150 mg/sqm iv on days 1 through 5. Repeat course q 4 weeks for 12 courses. Remove patients with progressive disease. Perform third look laparotomy on patients with no evidence of disease after 6 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VBL - 10 mg vials; BLEO - 15 unit ampules; CACP - 10 mg lyophilized cakes; ACT-D - 0.5 mg vials; VCR - 1 and 5 mg vials; CTX - 100, 200, and 500 mg vials.

DATE SUMMARIZED: 02/79

4.0032 PILOT CHEMOTHERAPY WITH MELPHALAN PLUS IMMUNOTHERAPY WITH LEVAMISOLE FOR STAGE III/IV OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) GOG-7891

OBJECTIVES:

I. Evaluate the feasibility and possible toxicity of combining melphalan chemotherapy with levamisole immunotherapy for women with advanced ovarian epithelial malignancies.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage III or IV ovarian cancer who have not had prior chemotherapy or radiotherapy and whose survival is estimated to be at least 3 months. Patients will have undergone surgical debulking of as much tumor as is prudent. Adequate bone marrow, renal and hepatic functions are required.

PROTOCOL OUTLINE: Nonrandomized study. Patients begin treatment following surgical debulking.

Single-agent Chemotherapy plus Immunotherapy. Melphalan, L-PAM, NSC-8806; plus Levamisole, LEV, NSC-177023.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: T and B cells, lymphocyte transformation, skin testing.

END POINTS: Duration of response, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

L-PAM - 7 mg/sqm po on days 1 through 5 (maximum dose for one course is 80 mg); LEV - 100 mg/sqm po in 2 divided doses on days 12, 13, 19, and 20. Repeat every 4 weeks. Any delay in the onset of Chemotherapy concomitantly delays subsequent LEV Immunotherapy (i.e., the time interval between L-PAM and LEV doses is constant). A minimum of 10 courses is required.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-PAM - 2 mg tablets; LEV - 50 mg tablets.

DATE SUMMARIZED: 08/80

4.0033 PHASE III CHEMOTHERAPY WITH ADR/CTX VS ADR/CTX/CACP FOR ADVANCED OVARIAN ADENOCARCINOMA

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PROTOCOL NUMBER(S) GOG-7961; GOG-47

OBJECTIVES:

I. Compare effect of combination chemotherapy with adriamycin (ADR) cyclophosphamide (CTX) vs. ADR/CTX/cis-platinum (CACP) on suboptimal Stage III, Stage IV, and recurrent ovarian adenocarcinoma.

PROTOCOL ENTRY CRITERIA: Patients 70 years of age or less, with FIGO Stage IV or suboptimal Stage III primary disease or recurrent disease (serous, mucinous, clear-cell or endometrioid adenocarcinoma; undifferentiated or mixed epithelial carcinoma). Patients must have: adequate hematologic function, normal renal function, and GOG performance of at least 3. Patients must not have: carcinoma of uncertain malignancy, prior cancer chemotherapy or radiotherapy, septicemia, severe infection, acute hepatitis, severe gastrointestinal bleeding.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm II: 3-Drug Combination Chemotherapy. ADR; CTX; cis-Platinum, CACP, NSC-119875.

STRATIFICATION: Participating institutions; GOG performance status: 0-1 vs. 2-3; measurability: yes vs. no.

SPECIAL STUDY PARAMETERS: Hematologic, liver, and kidney function; radiographic, palpable, and pelvic examination lesions; tumor measurement.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 400 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: ADR - 50 mg/sqm (maximum cumulative dose 400 mg/sqm); CTX - 500 mg/sqm.

Arm II: ADR and CTX as in Arm I; CACP - 50 mg/sqm.

Give all drugs iv using separate syringes on same day q 3 weeks for 8 courses. Evaluate response after third course. Remove patients with no response from chemotherapy, and continue chemotherapy for total of 8 courses or until disease progression for all other patients. Perform laparotomy on CRs, resectable PRs, and SDs (after hematologic recovery) in order to establish truly complete remission status. Follow all patients for 5 years. Maintain patients in complete remission following laparotomy, as well as those who refuse surgery or are medically inoperable: CTX - 500 mg/sqm (escalate by 25 percent per dose to a maximum of 1100 mg/sqm/dose) iv q 3 weeks until relapse or for a total of 12 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200, and 500 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 02/80

4.0034 PHASE I-II COMBINATION CHEMOTHERAPY WITH ADR/CTX PLUS RADIOTHERAPY AND SURGERY FOR OVARIAN CARCINOMA

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California, 94304, United States of America
PROTOCOL NUMBER(S) NCOG-5O83

OBJECTIVES:

I. Determine the patient tolerance to a combination of limited field irradiation plus adriamycin (ADR)/cyclophosphamide (CTX) in patients with ovarian carcinoma.

II. Gain experience with the use of this combined modality therapy in order to use it as first line therapy in future randomized trials.

PROTOCOL ENTRY CRITERIA: Patients between 21 and 75 years of age with biopsy proven primary serous, endometroid, mucinous, clear cell, mixed, undifferentiated or anaplastic carcinoma of the ovary, FIGO Stages I, II or asymptomatic III. Patients must have an adequate cardiac status, a Karnofsky performance status of 60 or more and must not have had prior pelvic or abdominal radiotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Surgery plus Radiotherapy plus 2-Drug Combination Chemotherapy. Radiotherapy at 4-25 MeV; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Lymphangiogram, IVP, CEA, peritoneoscopy.

END POINTS: Response/remission rate, objective tumor response, survival time, relapse-free interval, toxicity/morbidity of treatment, duration of response, recurrence rate.

CURRENT STATUS: 16 to 24 patients will be entered in 6 to 9 months.

DOSAGE SCHEDULE:

Stage I or II disease undergo total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy, otherwise remove as much of tumor as possible. Radiotherapy begins 4 to 10 weeks after and upon recovery from surgery. 4500 rad given in 33 to 50 days to the entire pelvis. Chemotherapy begins 4 weeks after completion of Radiotherapy. ADR - 50 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on day 1; CTX - 250 mg/sqm po on days 2 through 5. Repeat course q 21 days for 3 cycles, then q 4 weeks, as long as disease responds, up to 1 year. After 1 year, a second look surgery may be performed on patients in complete clinical remission. Remove from study patients in partial clinical remission or patients found to have residual disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules. CTX - 100 and 500 mg ampules.

DATE SUMMARIZED: 11/79

4.0035 AC (ADR/CTX) VS PAC (CACP/ADR/CTX) COMBINATION CHEMOTHERAPY FOR ADVANCED SURFACE EPITHELIAL CARCINOMA OF THE OVARY

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PROTOCOL NUMBER(S) NCOG-5O91

OBJECTIVES:

I. Compare AC (adriamycin/cyclophosphamide) with PAC (cis-platinum/adriamycin/cyclophosphamide) following debulking surgery for the treatment of Stage III-IV surface epithelial carcinoma of the ovary.

II. Determine the contribution of early, aggressive cytoreductive surgery where used in combination with chemotherapy in approaching the ovarian cancer patient with curative intent.

III. Evaluate the effectiveness of combination chemotherapy in patients with bulky, suboptimal disease (more than 2 cm) in comparison with patients with optimal residual disease (not more than 2 cm).

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven Stage III-IV malignant surface epithelial tumors of the ovary, including serous cystadenocarcinoma, mucinous cystadenocarcinoma, endometroid, clear cell, and undifferentiated/anaplastic. Patients must not be over the age of 80 years, must have a Karnofsky performance status of at least 60 percent, and must have adequate bone marrow and renal function. There may have been no prior malignancy within 7 years, excluding skin carcinoma, and there may be no history of significant pelvic or abdominal radiation therapy or systemic chemotherapy.

PROTOCOL OUTLINE: Randomized study. Regimen A is recommended for all patients. However, debulking Surgery, if not done prior to initiation of Chemotherapy, may be performed after 3 cycles of Chemotherapy in patients with stable or responding disease.

Regimen A: Surgery. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy with removal of all gross tumor.

Arm I: 2-Drug Combination Chemotherapy. AC: Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm II: 3-Drug Combination Chemotherapy. PAC: cis-Platinum, CACP, NSC-119875; ADR; CTX.

STRATIFICATION BY: Participating institutions, histologic type (serous cystadenocarcinoma vs. other), histologic grade (well vs. moderately vs. poorly differentiated), Karnofsky performance status (60-70 vs. 80-100), Stage (III vs. IV), residual disease after surgery and before chemotherapy (largest residual nodule more than 2 cm vs. not more than 2 cm).

SPECIAL STUDY PARAMETERS: Hematologic parameters, kidney and liver function tests, creatinine clearance, CEA, chest x-ray, IVP, abdominal/pelvic ultrasound and/or CT scan, audiometry, EKG.

END POINTS: Response/remission rate, duration of response, survival, duration of survival.

CURRENT STATUS: The estimated annual patient accrual is 52-61 for the projected 5.5 year study.

DOSAGE SCHEDULE:

Arm I: AC: ADR - 50 mg/sqm iv on day 1; CTX - 250 mg/sqm/day po on days 2 through 5. Repeat course q 4 weeks. Discontinue ADR after a total accumulated dose of 450 mg/sqm.

Arm II: PAC: CACP - 60 mg/sqm iv over 24 hours, with adequate prehydration and mannitol diuresis if necessary during treatment; ADR as in Arm I; CTX - 600 mg/sqm iv over 5-15 minutes. Repeat course q 4 weeks. Increase CTX to 800 mg/sqm after ADR has been discontinued because of maximum accumulated dose.

At the end of 12 cycles of treatment, patients will undergo diagnostic surgical evaluation. Patients with a complete response will go off treatment; those with progression will be declared failures. Patients with a partial response will continue on Chemotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules; CTX - 25 and 50 mg tablets; CACP - 10 mg vials.

DATE SUMMARIZED: 12/80

4.0036 PHASE III INDUCTION AND MAINTENANCE WITH ADR/CTX/BCG VS ADR/CTX/CACP VS ADR/CTX/CACP/BCG FOR STAGE III AND IV OVARIAN CANCER

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PROTOCOL NUMBER(S) SWOG-7925

OBJECTIVES:

I. Compare the effectiveness of the SWOG-7524 protocol best therapy arm: adriamycin (ADR)/cyclophosphamide (CTX)/BCG-Connaught (BCG) vs. ADR/CTX/cis-platinum (CACP) vs. ADR/CTX/CACP/BCG for remission induction and/or maintenance of disease-free status and prolongation of survival in patients with measurable and non-measurable ovarian carcinoma, Stages III and IV.

II. Compare the toxicities of these regimens.

PROTOCOL ENTRY CRITERIA: Patients less than 70 years of age with histologically confirmed optimal and sub-optimal Stage III or IV or recurrent epithelial type ovarian carcinoma. Patients must have had no prior nor concomitant malignancy nor cytotoxic chemotherapy nor pelvic radiation. Patients must have a performance status less than 3, adequate renal cardiac and hepatic functions and be entered less than 6 weeks following surgical exploration.

PROTOCOL OUTLINE: Randomized study, with randomization loading of 1:2:2 for Arms I, II and III respectively. Separately randomize patients with measurable vs. non-measurable disease.

Induction:

Arm I: 2-Drug Combination Chemotherapy plus Immunotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; plus BCG-Connaught, BCG, NSC-B116341.

Arm II: 3-Drug Combination Chemotherapy. ADR; CTX; cis-Platinum, CACP, NSC-119875.

Arm III: 3-Drug Combination Chemotherapy plus Immunotherapy. ADR; CTX; CACP; plus BCG.

STRATIFICATION: Participating institutions, performance status: optimal (0-1) vs. suboptimal (2-3).

SPECIAL STUDY PARAMETERS: CAT or sonogram scan; renal function tests; liver function tests.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, survival rate, recurrence rate.

CURRENT STATUS: 180 patients will be entered.

DOSAGE SCHEDULE: Employ full doses of drugs in patients with adequate bone marrow reserve. Reduce dosage schedule for patients with impaired bone marrow reserve (IBMR), with gradual escalation to full dosages as tolerated.

Arm I: ADR - 40 mg/sqm iv on day 1 (30 mg/sqm for IBMR, maximum dose - 480 mg/sqm; CTX - 200 mg/sqm po on days 3 through 6 (150 mg/sqm for IBMR); BCG by scarification on days 8 and 15.

Arm II: ADR, CTX as in Arm I; CACP - 50 mg/sqm iv on day 1.

Arm III: ADR, CTX, BCG as in Arm I; CACP as in Arm II.

On all arms, give course q 3 weeks for the first 3 courses, then q 4 weeks for 12 courses for remission induction. Give at least 2 courses of therapy prior to removal from study due to disease progression. Perform second-look laparotomy on patients clinically NED at end of 12 courses and discontinue therapy for complete responders. Remove patients with disease progression following 12 courses of therapy and place on a second-line therapy protocol. Follow up all patients for life.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules; CTX - 50 mg tablets; BCG - 40 mg vials.

DATE SUMMARIZED: 11/79

4.0037 COMBINATION CHEMOTHERAPY WITH CACP/ADR/CTX/VP-16 FOR STAGE III/IV OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) BCRP-7924

OBJECTIVES:

I. Determine the efficacy of cis-platinum/adriamycin/cyclophosphamide/VP-16213 in the treatment of FIGO Stage III and Stage IV epithelial tumors of the ovary.

II. Determine the overall survival of these patients treated with this 4-drug combination.

III. Assess the toxicities associated with this therapeutic regimen.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven FIGO Stage III or IV epithelial ovarian tumors who have measurable disease or with whom there is an understanding that a second-look operation may be needed. The minimum expected survival must be at least 8 weeks. Patients may have received minimal prior local radiotherapy. There must be no history of a previous second primary malignant neoplasm. Patients should have undergone adequate surgical debulking prior to entry or give consent to undergo such debulking prior to initiation of therapy.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; VP-16213, VP-16; NSC-141540.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-6, SMA-12, chest x-ray, lung tomography of suspicious lesions, bone x-rays as indicated, UGI and IVP if indicated, liver/spleen scan for suspected hepatic metastasis, bone scan and brain CAT scan if indicated, EKG, bone marrow aspirate and biopsy for abnormal hemogram or unexpected myelosuppression, culdocentesis.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

CACP - 50 mg/sqm iv on day 1 with adequate hydration and diuresis; ADR - 30 mg/sqm (maximum cumulative dose 540 mg/sqm) iv over 1 hour on day 1; CTX - 600 mg/sqm iv push on day 1; VP-16 - 100 mg/sqm iv over 60 minutes on days 1, 3, and 5. Repeat course q 28 days. If necessary, after total maximum dose of ADR has been reached, Methotrexate may be substituted at 40 mg/sqm iv on day 1.

All patients will receive a minimum of 2 courses of treatment and will continue on treatment as long as disease is stable or there is evidence of response. Second-look operation for evaluation of nonmeasurable disease in Stage III patients should be performed after the completion of 15 courses. If disease remains, an additional 12 courses should be administered and a third look undertaken at that time. If there is no disease at second look, Chemotherapy will be discontinued and the patient followed prospectively. Stage IV patients who achieve CR will continue to receive therapy for 2 years, after which therapy will be discontinued.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

4.0038 CHEMOTHERAPY WITH HCAP (CTX/ADR/CACP/HMM) VS CP (CTX/CACP) FOR STAGE III AND IV OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) MAYO-806151

OBJECTIVES:

I. Compare the therapeutic index of combination chemotherapy with HCAP (cyclophosphamide/adriamycin/cis-platinum/hexamethylmelamine) with that of combination chemotherapy with CP (cyclophosphamide/cis-platinum) in Stage III and IV ovarian carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed F.I.G.O. Stage III or IV ovarian carcinoma. Patients must have an expected survival of at least 2 months, an ECOG performance status of at least 3, and adequate renal, hematologic, hepatic, and cardiac function. Patients must have recovered from prior surgery, radiation, or chemotherapy. Chemotherapy must not have been with any of the protocol drugs. Patients must not have significant infections or other active cancer (except non-melanoma skin).

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. CP: Cyclophosphamide, CTX, NSC-26271; cis-Platinum, CACP, NSC-119875.

Arm II: 4-Drug Combination Chemotherapy. HCAP: CACP, CTX; Adriamycin, ADR, NSC-123127; Hexamethylmelamine, HMM, NSC-13875.

STRATIFICATION BY: Age: 49 or under vs. 50 or older; histologic grade: 1 or 2 vs. 3 or 4; performance status: 0 or 1 vs. 2 or 3; gross extent of residual disease: none vs. minimal vs. extensive vs. massive.

SPECIAL STUDY PARAMETERS: Tumor measurements; chest x-ray; hematologic, renal, and hepatic function tests.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 72 evaluable patients per arm will be required for statistical validity.

DOSAGE SCHEDULE:

Arm I: CP: CTX - 1000 mg/sqm iv push on day 1; CACP - 60 mg/sqm iv over 2 hours with mannitol on day 1.

Arm II: HCAP: CTX - 400 mg/sqm iv push on day 1; ADR - 30 mg/sqm iv over 5-10 minutes on day 1 (total cumulative dose not to exceed 500 mg/sqm); CACP - 60 mg/sqm iv over 2 hours with mannitol on day 1; HMM - 150 mg/sqm po in 3 divided doses on days 2-8.

Treatment will continue for at least 12 monthly courses unless progression occurs earlier. After 1 year, patients with CR stop treatment; those with stable disease continue treatment until CR or progression. Patients go off study any time progression is observed.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; ADR - 10 mg vials; CACP - 10 mg vials; HMM - 50 and 100 mg capsules.

DATE SUMMARIZED: 06/80

4.0039 COMBINATION CHEMOTHERAPY WITH L-PAM/CACP VS HAC (HMM/ADR/CTX) FOR STAGES III AND IV EPITHELIAL OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) MDAR-301; MDA-G-7804

OBJECTIVES:

I. Define the activity of cis-platinum (CACP) and melphalan (L-PAM) in combination vs. HAC - hexamethylmelamine (HMM), adriamycin (ADR) and cyclophosphamide (CTX).

II. Study the effect of tumor reductive surgery as an adjunct to chemotherapy.

III. Study and compare drug activity in comparable clinical situations.

PROTOCOL ENTRY CRITERIA: Patients with a histological diagnosis of common epithelial ovarian cancer of serous, mucinous, endometrioid, clear cell or mixed histological type. Patients must have had a definitive laparotomy including staging, documentation of tumor volume and extent, and 'maximum effort' surgical tumor volume reduction. Patient must have adequate bone marrow, renal, and hepatic function.

PROTOCOL OUTLINE: Randomized study. Cross over nonresponders (NR) to the alternate therapy.

Arm I: 2-Drug Combination Chemotherapy. Melphalan, L-PAM, NSC-8806; cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy. HAC: Hexamethylmelamine, HMM, NSC-13875; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: Residual tumor volume, histological grade.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response.

CURRENT STATUS: 75 to 100 patients will be entered per year.

DOSAGE SCHEDULE:

Arm I: L-PAM - 0.2 mg/kg/day po on days 1 through 5; CACP - 20 mg/sqm iv on days 2, 3 and 4 (length of course and number of courses are not given).

Arm II: HAC: HMM - 4 mg/kg po on days 1 through 14; ADR - 40 mg/sqm iv on day 1 (discontinue after 450 mg/sqm.); CTX - 200 mg/sqm po on days 1 through 5. Repeat course q 4 weeks. Cross over nonresponders to alternate therapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/79

4.0040 SINGLE-AGENT THERAPY WITH L-PAM OR CACP AND COMBINATION CHEMOTHERAPY WITH HMM/CTX/ADR FOR ADVANCED CANCER OF THE OVARY

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PROTOCOL NUMBER(S) MDAR-64; MDA-13; MDA-14

OBJECTIVES:

I. Identify chemotherapy agents that are effective in the treatment of ovarian cancer.

II. Compare the efficacy of the alkylating agent melphalan (L-PAM) with following drugs and drug combinations: cis-Platinum, hexamethylmelamine plus cytoxan; hexamethylmelamine, cytoxan plus adriamycin.

PROTOCOL ENTRY CRITERIA: Patients with measurable lesions of advanced epithelial cancers (serous, mucinous, undifferentiated, adenocarcinoma, endometrioid and mesonephric) of the ovary previously untreated by chemotherapy. Ovarian carcinomas FIGO Stages III and IV are eligible.

PROTOCOL OUTLINE: Randomized study. Patients are initially randomized to Arms I, II, III, and IV. Failures may cross over to another arm. Patients who do not respond to initial treatment and subsequent cross-over treatment are rerandomized to Arms V and VI. Rerandomization is affected by the drugs received during initial therapy.

Induction:

Arm I: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm II: 2-Drug Combination Chemotherapy. Hexamethylmelamine, HMM, NSC-13875; Cyclophosphamide, CTX, NSC-26271. Nonresponders cross over to Arm IV.

Arm III: 3-Drug Combination Chemotherapy. HMM, CTX, Adriamycin, ADR, NSC-123127. Nonresponders cross over to Arm I.

Arm IV: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875. Nonresponders cross over to Arm II.

Arm V: Single-agent Chemotherapy. ADR.

Arm VI: Single-agent Chemotherapy. CACP.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, remission duration, objective tumor response.

CURRENT STATUS: 100 patients will be entered in one year.

DOSAGE SCHEDULE:

Arm I: L-PAM - 0.2 mg/kg/day po for 5 days q 4 weeks. Number of courses not given. Enter nonresponders in Arm V or Arm VI.

Arm II: HMM - 4 mg/kg/day on days 1 through 14 q 4 weeks; CTX -200 mg/sqm/day on days 1 through 5 q 4 weeks. Repeat course and evaluate patients at 8 weeks. Enter nonresponders in Arm IV.

Arm III: HMM and CTX, as in Arm II, plus ADR - 40 mg/sqm iv on day 1 q 4 weeks. Maximum cumulative dose - 450 mg/sqm.

Arm IV: CACP - 30 mg/sqm/day iv given over 4 hours on days 1, 2 and 3 q 4 weeks.

Number of courses not given. Enter nonresponders in Arm II. Additional cross-over. Enter patients with enlarging tumor after any of the above regimens in Arm V or Arm VI, if drug has not been used previously.

Arm V: ADR - 40 mg/sqm iv on day 1 q 4 weeks.

Arm VI: CACP - as in Arm IV.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 04/76

4.0041 CHEMOTHERAPY WITH CTX, ADR, CACP, AND CLB FOR ADVANCED OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) MSKCC-7931

OBJECTIVES:

I. Compare the effect of combination versus sequential administration of cyclophosphamide (CTX), cis-Platinum (CACP), and adriamycin (ADR).

II. Compare the results of various marker studies with the clinical course of patients treated under this protocol.

PROTOCOL ENTRY CRITERIA: Patients not over 70 years old with Stage III or IV epithelial ovarian carcinoma. Patients must have had adequate surgery including debulking, must have a performance status of 50 or better, and must not have had prior radiation or chemotherapy.

PROTOCOL OUTLINE: Randomized study. Patients are randomized to Arms I and II following debulking Surgery including TAH, BSO and omentectomy. Arm I nonresponders enter Regimen A; Arm I responders enter Regimen B.

Arm I: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm II: 3-Drug Combination Chemotherapy. CTX; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Regimen A: 2-Drug Combination Chemotherapy. ADR; CACP.

Regimen B: Single-agent Chemotherapy. Chlorambucil, CLB, NSC-3088.

STRATIFICATION: Residual disease: more vs less than 1 cm; Broder's histologic grade: I and II vs III and IV; place of surgery: Memorial Hospital vs elsewhere.

SPECIAL STUDY PARAMETERS: Skin tests for recall antigens; CEA assay; 5-prime nucleotides; IVP; barium enema; estrogen and progesterone receptor assay; ovarian carcinoma antigen assay; bone, liver and brain scans; audiogram; clonogenic culture and drug sensitivity of primary and subsequent tumor specimens.

END POINTS: Response/remission rate, disease-free interval, quality of life, survival time, objective tumor response.

CURRENT STATUS: 80 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: CTX - 1000 mg/sqm on day 1 q month for 1 year. Enter patients with residual or progressive disease to Regimen A. Perform second look surgery in patients with no evidence of disease (NED). If NED, enter patients to Regimen B.

Arm II: CTX - 750 mg/sqm iv on day 1 q 4 weeks (reduce dose to 600 mg/sqm when administered with CACP on weeks 0, 8, 16 and 24) for 36 weeks, then increase dose to 1000 mg/sqm given q 4 weeks to week 52; CACP - 120 mg/sqm iv on day 1 q 8 weeks for 4 courses; ADR - 50 mg/sqm (total cumulative course 480 mg/sqm) iv on day 1 q 4 weeks (reduce dose to 40 mg/sqm when administered with CACP on weeks 0, 8, 16 and 24) for 36 weeks. After 1 year remove from study patients with progressive or residual disease. IF NED is verified by second look laparotomy, discontinue therapy and observe patients until disease progression, then remove from study.

Regimen A: Enter nonresponders from Arm I. ADR - 50 mg/sqm iv on day 1 q 4 weeks for 10 weeks (reduce dose to 40 mg/sqm when administered with CACP on weeks 0, 8, 16 and 24); CACP - 120 mg/sqm iv on day 1 q 8 weeks for 4 courses. Remove from the study patients with progressive or residual disease. Perform second look laparotomy for patients with NED.

Regimen B: Enter responders from Arm I. CLB - 6 mg/sqm/day po for 1 year. Cross over patients failing on this Arm to Arm II therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

4.0042 CHEMOTHERAPY WITH L-PAM FOR SELECTED STAGE I AI OR BI OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) OCSG-7601

OBJECTIVES:

I. Define the natural history (relapse rate, relapse sites, relapse-free survival) in patients with carcinoma of one or both ovaries potentially cured by surgery.

II. Determine whether prophylactic, adjuvant chemotherapy with melphalan (L-PAM) alters the natural history.

III. Study the effect of various potential prognostic factors (stratification factors) on the natural history of patients treated by each form of therapy.

IV. Determine the patterns of relapse for each form of therapy.

V. Establish the value of various staging parameters on the stages of disease and its natural history.

PROTOCOL ENTRY CRITERIA: Patients previously untreated except by surgery with histologically confirmed, well or moderately differentiated epithelial (serous, mucinous or other) ovarian cancer. Patients must have adequate bone marrow, renal and hepatic function, and must have undergone a staging laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm II: Control Group. No treatment.

STRATIFICATION BY: Histological type, histological grade; tumor stage; participating institutions.

SPECIAL STUDY PARAMETERS: Lymphangiogram, staging laparotomy.

END POINTS: Recurrence rate, survival time, relapse site, relapse-free interval.

CURRENT STATUS: 50 patients will be entered.

DOSAGE SCHEDULE:

Arm I: L-PAM - 0.2 mg/kg/day po on days 1 through 5 q 4 weeks for 18 months. Chemotherapy will be discontinued at 18 months if the patient is free of disease. At 18 months, the patient will undergo second-look peritoneoscopy and/or laparotomy. Remove patients who relapse from study.

Arm II: No therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/78

4.0043 CHEMOTHERAPY WITH RADIOACTIVE CHROMIC PHOSPHATE VS L-PAM WITH OR WITHOUT RADIOTHERAPY FOR STAGE I AND II OVARIAN CANCER

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PROTOCOL NUMBER(S) OCSG-7602

OBJECTIVES:

I. Define the natural history (relapse rate, relapse sites, relapse-free survival, regression rate, duration of regression of patients treated by surgery plus either chemotherapy or chemotherapy plus radiation therapy in definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings (Stages IC, IIA, IIB, IIC), and in those Stage IAi and IBi patients with poorly differentiated tumors, and in Stage IAii and IBii patients.

II. Study the effect of various potential prognostic factors (stratification factors) on the natural history of patients treated by each form of therapy.

III. Determine the patterns of relapse for each form of therapy.

IV. Establish the value of various staging parameters on the stage of disease and its natural history.

PROTOCOL ENTRY CRITERIA: Postsurgical patients curatively resected for epithelial ovarian cancer, Stages IC, IIA, IIB, IIC, or IAi, IBi with poorly differentiated tumor or Stages IAii, IBii, with histological diagnosis of serous, mucinous or other endometrioid, transitional, mesonephroid (clear cell), adenocanthoma (endometrioid with squamous metaplasia), mixtures and intermediate types and unclassifiable (undifferentiated) and histologically graded as well, moderately or poorly differentiated. Patients must not have had prior radiation or chemotherapy and must have adequate bone marrow, renal and hepatic function. All patients undergo staging laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy.

PROTOCOL OUTLINE: Randomized study. Randomize resectable Stage II and poor-prognosis Stage I patients to Arms I or II. Randomize incompletely resected Stage IIB and IIC patients to Arms I or II.

Arm I: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm II: Isotope Therapy. Intra-abdominal radioactive Chromic phosphate.

Arm III: Radiotherapy plus Single-agent Chemotherapy. Megavoltage or Cobalt-60; L-PAM.

STRATIFICATION BY: Cell type: serous, mucinous, others as specified; histological grade: well, moderately vs. poorly differentiated; FIGO Stage; residual disease: presence and extent.

SPECIAL STUDY PARAMETERS: IVP, lymphangiogram, staging laparotomy.

END POINTS: Response/remission rate, objective tumor response, relapse rate, relapse sites, relapse-free survival, regression rate, duration of regression, survival rate.

CURRENT STATUS: 60-90 patients will be entered.

DOSAGE SCHEDULE:

Arm I: L-PAM - 0.2 mg/kg/day po for 5 days q 4 weeks for 18 months.

Arm II: Radioactive Chromic phosphate - 7.5 mCi by abdominal infusion, administered 1-2 weeks postoperatively.

Arm III: L-PAM, as in Arm I, plus Radiotherapy to start within 4 weeks postoperatively - 4000 rad given in 4-5 weeks to entire pelvis. Give patients with residual disease greater than 2.0 cm an additional 1000 rad to residual tumor by reduced fields.

Perform second-look operation on all responders free of disease after 18 months of Chemotherapy within 2 months of completion of this therapy. Remove patients with disease progression from study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/78

4.0044 CHEMOTHERAPY WITH ACT-D/5-FU/CTX, MTX/CF/CTX, AND VCR/ADR, AND MTX/CF AND C. PARVUM IMMUNOTHERAPY FOR EPITHELIAL OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) OCSG-7603; RPMI-7603

OBJECTIVES:

I. Define the natural history (rate and duration of regression and survival) and patterns of relapse of definitively staged patients during treatment by various chemotherapeutic and immunotherapeutic regimens for surgically inoperative ovarian cancer which extends beyond the pelvic region.

II. Study the effects of various potential prognostic factors (stratification factors), and establish the value of various staging parameters on the stage of disease, for the natural history of patients treated by each form of therapy.

III. Determine the value of various immunological parameters (including circulating specific cystadenocarcinoma antigen) as potential prognostic and surveillance factors in the natural history of patients treated by each form of therapy, and determine if non-specific immunotherapy influences the immunologic parameters.

IV. Determine the value of simple surgical biopsy vs. reductive tumor surgery as the initial surgical approach.

V. Attempt correlation of the therapeutic response and toxicity of methotrexate with serum and effusion levels.

PROTOCOL ENTRY CRITERIA: Patients with epithelial ovarian cancers of the following types: serous cystomas, mucinous cystomas and others including mixed serous and mucinous endometroid, clear cell and malignant Brenner undifferentiated tumor, but not including mixed mesodermal tumor.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. ACFUCY: Actinomycin-D, ACT-D, NSC-3053; 5-Fluorouracil, 5-FU, NSC-19893; Cyclophosphamide, CTX, NSC-26271.

Arm II: 3-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590; CTX.

Arm III: 2-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127.

Arm IV: 2-Drug Combination Chemotherapy. High-dose MTX-CF alone. MTX; CF.

Arm V: Immunotherapy. Corynebacterium parvum, C. parvum, NSC-220537.

STRATIFICATION BY: Histological type, grade and extent of differentiation of tumor, modified FIGO staging, presence of measurable disease, degree of prior surgery, prior chemotherapy, delayed hypersensitivity skin tests.

SPECIAL STUDY PARAMETERS: BUN, creatinine, SMA-12, serologic tests, skin tests, RIA for serum MTX level, lymphocyte stimulation tests (PHA and concanavalin A) leukocyte migration inhibition testing against purified cystadenocarcinoma antigen, RIA for serum cystadenocarcinoma antigen, circulating immunoglobulin.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, pattern of tumor relapse.

CURRENT STATUS: 89 patients have been entered.

DOSAGE SCHEDULE:

Arm I: ACT-D - 0.5 mg 1 day iv on days 1 through 5. 5-FU - 280 mg/sqm/day iv on days 1 through 5. CTX - 250 mg/sqm/day iv on days 1 through 5 (single dose not to exceed 500 mg). Repeat course q 4 weeks.

Arm II: MTX - 500 mg/sqm iv during 4 hours followed 6 hours later by rescue with CF - 10 mg/sqm im q 6 hours x 12. CTX - 250 mg/sqm iv on days 1 through 5 beginning after MTX infusion (single dose not to exceed 5000 mg). Decrease MTX to 700 mg/sqm after 4 weeks in absence of tumor response and if toxicity is absent. Repeat courses q 4 weeks.

Arm III: VCR - 1.2 mg/sqm iv single dose 6 hours prior to ADR. ADR - 60 mg/sqm iv single dose. Repeat course q 4 weeks.

Arm IV: MTX-CF as in Arm II.

Arm V: C. parvum - 2.0 mg iv during 45-60 minutes x 12 q 4 weeks, x 4 q 8 weeks and all succeeding doses q 12 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: C. parvum - 7 mg ampule; others not given.

DATE SUMMARIZED: 01/77

4.0045 COMBINATION CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE, ADRIAMYCIN AND CIS-PLATINUM FOR ADVANCED OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) SFCC-78070

OBJECTIVES:

I. Assess the acute and chronic toxicities of an alternating combination chemotherapy program employing two drug combinations, cyclophosphamide (CTX)/adriamycin (ADR) and CTX/cisplatinum (CACP), in patients with advanced ovarian carcinoma.

II. Determine the complete response rate and its duration using the above combination regimens in patients with advanced ovarian carcinoma after optimal surgical treatment.

III. Compare the sensitivity of noninvasive methods of assessing residual tumor with laparoscopy and laparotomy at the conclusion of a combined-modality treatment.

IV. Obtain tumor tissue to investigate the origins and mechanisms of drug resistance and to prepare specific antisera to human ovarian carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed common epithelial carcinoma of the ovary (serous, mucinous, endometrioid, and poorly differentiated or undifferentiated adenocarcinoma and clear cell carcinoma) F.I.G.O. Stages III and IV or patients with recurrent ovarian carcinoma and anatomic spread consistent with Stage III or IV designation.

PROTOCOL OUTLINE: Nonrandomized study. All patients undergo initial surgery.

2-Drug Combination Chemotherapy alternating with 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127 plus Cyclophosphamide, CTX, NSC-26271 alternating within CTX plus cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: CEA, IVP, abdominal ultrasound, peritoneal lymphoscintigraphy, abdominal CT scan, staging laparoscopy and laparotomy.

END POINTS: Response/remission rate, duration of response, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

ADR - 70 mg/sqm plus CTX - 75 mg/sqm given through a freely running scalp vein iv over 15 to 30 min on day 1; alternating with CTX - 75 mg/sqm iv given on day 21 plus CACP - 20 mg/sqm iv on days 21 through 25 with adequate hydration. Repeat q 6 weeks for a total of 4 courses in 6 months. Perform laparoscopy on patients with initially minimal disease after 2 courses of each combination to determine response and re-evaluate after 2 more full courses. Evaluate candidates for secondary surgical cytoreduction after each cycle of Chemotherapy, and follow any subsequent Surgery with 4 full courses of Chemotherapy, then restage patients. Enter patients without measurable disease to Immunotherapy protocol without further Chemotherapy. Re-evaluate all patients q 3 months. Repeat Induction therapy or enter to alternate treatment patients with recurrent disease.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/79

4.0046 POSTOPERATIVE RADIOTHERAPY PLUS MELPHALAN VS RADIOTHERAPY PLUS MELPHALAN PLUS BCG IMMUNOTHERAPY FOR OVARIAN CANCER

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PROTOCOL NUMBER(S) WI-MCW-OV-1

OBJECTIVES:

I. Compare the response of patients with ovarian cancer of Stages I-A, I-B, I-C, II, and III to postoperative radiotherapy plus melphalan vs. radiotherapy plus melphalan plus BCG immunotherapy.

II. Define the natural history of patients treated by standard radiotherapy and chemotherapy and study the effects of various potential prognostic factors on the natural history of patients treated by each form of therapy.

III. Determine the degree of antigenicity of ovarian epithelial cancer.

IV. Determine the patterns of relapse and remission for each form of therapy.

PROTOCOL ENTRY CRITERIA: Patients with a histopathologic diagnosis of ovarian cancer (serous, mucinous, or other) in Stages I-A, I-B, I-C, II, or III who have undergone surgical resection but who have not received prior radiotherapy or chemotherapy. Bone marrow, hepatic, and renal functions must be adequate, and the expected survival must be at least 2 months. There may be no prior history of cancer aside from skin cancer.

PROTOCOL OUTLINE: Randomized study. Patients are randomized to Arms I and II within 2 weeks of laparotomy.

Arm I: Single-agent Chemotherapy plus Radiotherapy. Melphalan, L-PAM, NSC-8806; plus Megavoltage Radiotherapy, including Co-60.

Arm II: Single-agent Chemotherapy plus Radiotherapy plus Immunotherapy. L-PAM; Megavoltage Radiotherapy; plus BCG, unspecified, BCG.

STRATIFICATION BY: Tumor histology (serous vs. mucinous vs. other), histologic grade (Grade 1 vs. well differentiated vs. poorly differentiated), prior surgical therapy (biopsy vs. tumor-reductive surgery vs. surgery outside the protocol), measurable disease (yes vs. no).

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-12, liver and kidney function studies, chest x-ray, IVP, barium enema, bone scan, liver/spleen scan, proctoscopy, cystoscopy.

END POINTS: Tumor relapse, disease-free interval, survival.

CURRENT STATUS: About 25 patients per arm will be required.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 5000 rads pelvic and whole abdominal irradiation beginning within 4 weeks of surgery; L-PAM - 0.2 mg/kg/day po for 5 consecutive days; begin after completion of Radiotherapy and repeat monthly for 12 courses or until progression.

Arm II: Radiotherapy and L-PAM as in Arm I; BCG - 400 x 10 to the sixth CFU id weekly for the first month beginning within 2 weeks of surgery, then monthly as long as patient is in remission, with decreasing doses depending on the biological response to the previous dose as indicated by local reaction.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

4.0047 POSTOPERATIVE MELPHALAN VS MELPHALAN PLUS BCG IMMUNOTHERAPY FOR STAGE III-IV OVARIAN CANCER

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PROTOCOL NUMBER(S) WI-MCW-OV-2

OBJECTIVES:

I. Compare the response of Stage III-IV ovarian cancer patients to postoperative melphalan vs. melphalan plus BCG immunotherapy.

II. Define the natural history of patients treated by standard chemotherapy and study the effects of various potential prognostic factors on the natural history of patients treated by each form of therapy.

III. Determine the degree of antigenicity of ovarian epithelial cancer.

IV. Determine the patterns of relapse and remission for each form of therapy.

PROTOCOL ENTRY CRITERIA: Patients with a histopathologic diagnosis of Stage III-IV ovarian cancer (serous, mucinous, or other) who have undergone surgical resection or biopsy but who have not received prior radiotherapy or chemotherapy. Bone marrow, hepatic, and renal functions must be adequate, and the expected survival must be at least 2 months. There may be no prior history of cancer aside from skin cancer.

PROTOCOL OUTLINE: Randomized study. Patients are randomized to Arms I and II within 2 weeks of surgery.

Arm I: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm II: Single-agent Chemotherapy plus Immunotherapy. L-PAM; plus BCG, unspecified.

STRATIFICATION BY: Tumor histology (serous vs. mucinous vs. other), histologic grade (Grade 1 vs. well differentiated vs. poorly differentiated), prior surgery (biopsy only vs. tumor reductive surgery vs. surgery outside the protocol), measurable disease (yes vs. no).

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-12, liver and kidney function tests, chest x-ray, IVP, barium enema, bone scan, liver/spleen scan, proctoscopy, cystoscopy.

END POINTS: Tumor relapse, disease-free interval, survival.

CURRENT STATUS: About 45 patients will be entered on each arm.

DOSAGE SCHEDULE:

Arm I: L-PAM - 0.2 mg/kg/day for 5 consecutive days. Begin therapy within 2 weeks of Surgery and repeat courses monthly for a total of 12 courses or until progression.

Arm II: L-PAM - as in Arm I; BCG - 400 x 10 to the sixth CFU id weekly for the first month beginning within 2 weeks of Surgery, then monthly as long as patient is in remission, with decreasing doses depending on the biological response to the previous dose as indicated by local reaction.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

4.0048 ADJUVANT RADIOTHERAPY, RADIOACTIVE CHROMIC PHOSPHATE AND MELPHALAN FOR LIMITED CARCINOMA OF THE OVARY

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PROTOCOL NUMBER(S) CAN-NCIC-CG-7502; CANADA-5; CAN-NCIC-5; CAN-NCIC-OV2

OBJECTIVES:

I. Compare chemotherapy with L-PAM vs. radiocolloid therapy with chromic phosphate-P32 vs. radiotherapy to the pelvis for postsurgical patients with carcinoma of the ovary, Stages I, II, or IIIo.

II. For patients at high risk of recurrence, determine the value of therapy with chromic phosphate or with L-PAM, or with abdominal irradiation, when preceded by pelvic irradiation.

PROTOCOL ENTRY CRITERIA: Patients over 16 years of age with histologically confirmed, epithelial-cell carcinoma of the ovary who have undergone total abdominal hysterectomy with bilateral salpingo-oophorectomy. Include Stages I, II or III (modified Figo system).

PROTOCOL OUTLINE: Randomized study.

Separate randomization for low-risk (A) and high-risk (B) groups. Group B patients have Stage IIB or IIIo disease with tumor involvement confined to the pelvis, or Stage I or IIa disease together with one of the following: rupture of malignant ovarian cyst; cytological dedifferentiation (Grade III and IV); extra cystic excrescences; or positive peritoneal cytology. Randomize Group A patients to Arms I, II, or III, and Group B patients to Arms IV, V, or VI. (Protocol closed to patients at low risk March 1977.)

Arm I: Radiotherapy. Supervoltage to the pelvis. Arm closed March 1977.

Arm II: Radiocolloid Therapy. Colloidal radioactive Chromic phosphate (P32) administered intra-abdominally. Arm closed March 1977.

Arm III: Single-agent Chemotherapy. L-PAM, NSC-8806. Arm closed March 1977.

Arm IV: Radiotherapy. Irradiation of the pelvis and abdomen.

Arm V: Radiotherapy plus Radiocolloid Therapy. Supervoltage irradiation plus radioactive Chromic phosphate. (Arm closed April 1980 because of unacceptable toxicity.)

Arm VI: Radiotherapy plus Single-agent Chemotherapy. Supervoltage plus L-PAM.

STRATIFICATION BY: Participating institutions; risk groups (low vs. high).

SPECIAL STUDY PARAMETERS: I.V.P., barium enema.

END POINTS: Response/remission rate; relapse rate; mean time to relapse; survival rate; toxicity/morbidity of treatment.

CURRENT STATUS: Approximately 300 patients will be entered. High-risk (B) arms admitted 137 patients by September 30, 1978.

DOSAGE SCHEDULE:

Group A. Protocol closed to this group March 1977, because of low rate of accrual.

Arm I: Radiotherapy - 4000 to 4500 rads to entire pelvis over 4 weeks using parallel opposed or multiple fields. Begin therapy 4 to 8 weeks after Surgery.

Arm II: Radioactive colloidal Chromic phosphate-P32 - 15 millicuries within 1 to 4 weeks after Surgery.

Arm III: L-PAM - 8.0 mg/sqm/day po on days 1 through 4 q 4 weeks beginning 4 weeks after surgery. Total maximum dose per course - 70 mg. Continue Chemotherapy for 18 months or until recurrence.

Group B:

Arm IV: Treatment centers will elect to use either Procedure (1) or (2) for abdominal Radiotherapy. 4 to 8 weeks following Surgery give all patients 2250 rads midline dose in 12 to 14 days to pelvis, Cobalt or higher energy proton beam, technique as in Arm I, followed by abdominal irradiation: (1) 2250 rads midplane by a moving strip field technique over 8 to 10 weeks, or (2) 2250 rads midplane to entire peritoneal cavity using 2 large parallel opposed fields (Cobalt or megavoltage) given over 4.5 weeks. Shield kidneys to receive no more than 1800 rads.

Arm V: Arm I Radiotherapy to pelvis, followed by Arm II Radiocolloid Therapy. Arm closed April 1980 because of unacceptable toxicity.

Arm VI: Arm I Radiotherapy to pelvis, followed within 4 weeks by Arm III Chemotherapy with L-PAM.

Patients with disease progression may be entered to alternate therapeutic modality. Follow up all patients q 2 months for 18 months then q 3 months to 3 years, then q 6 months to 5 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

4.0049 COMPARISON OF L-PAM VS L-PAM/HMM AFTER FAILURE ON ADR/CACP FOR STAGE III-IV OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) CAN-NCIC-OV4

OBJECTIVES:

I. Document the response rate of ovarian cancer to postoperative combination chemotherapy with adriamycin/cis-platinum in patients with Stage III-IV disease.

II. Determine the durability of CR following adriamycin/cis-platinum therapy.

III. Compare the therapeutic efficacies and toxicities of melphalan and melphalan plus hexamethylmelamine in the treatment of patients who have failed on adriamycin/cis-platinum.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage III/IV epithelial cancer of the ovary who have not received prior chemotherapy or radiotherapy and whose expected survival is at least 3 months. Bone marrow, kidney, and liver functions must be adequate, and there may be no concurrent serious illness or cardiac disease.

PROTOCOL OUTLINE: Study randomized for nonresponders to initial Surgery and Chemotherapy in Regimens A and B.

Regimen A: Surgery. Staging and Cytoreduction.

Regimen B: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Regimen C: Surgery. Second-look procedure.

Arm I: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm II: 2-Drug Combination Chemotherapy. L-PAM; Hexamethylmelamine, HMM, NSC-13875.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, chest x-ray, EKG.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival.

CURRENT STATUS: About 300 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Maximal tumor reduction and measurement of residual disease.

Regimen B: ADR - 50 mg/sqm slow iv push; CACP - 50 mg/sqm iv over 2 hours with adequate hydration and mannitol diuresis. Repeat courses q 3-4 weeks for a total of 9 courses. Enter patients without clinical evidence of disease and those with PR or no change after 9 courses to Regimen C. If progressive disease develops after at least 3 courses, randomize patients to Arms I and II.

Regimen C. Second-look Surgery. If no evidence of disease is seen, patients are followed without further therapy; if evidence of tumor is encountered, maximal tumor reduction is carried out and patients randomized to Arms I and II.

Arm I: L-PAM - 8 mg/sqm/day po for 4 days; repeat courses q 4 weeks for a total of 12 courses.

Arm II: L-PAM - 6 mg/sqm/day po for 4 days; HMM - 120 mg/sqm/day po for 14 days. Repeat courses q 4 weeks for a total of 12 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

4.0050 L-PAM VS HAM (HMM/ADR/L-PAM) CHEMOTHERAPY FOR RESIDUAL EPITHELIAL OVARIAN CANCER WITH CACP FOR NONRESPONDERS

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PROTOCOL NUMBER(S) CAN-NCIC-7701; CAN-NCIC-OV3

OBJECTIVES:

I. Study the influence of residual tumor volume and chemotherapy on Stage III and IV ovarian carcinoma after cyto-reductive surgery.

II. Attempt to accentuate responses to melphalan by adding adriamycin and hexamethylmelamine in melphalan responders.

III. Determine the response rate of patients with ovarian carcinoma to cis-platinum after failure of initial chemotherapy.

IV. Study whether the information gained by performing laparoscopy after 6 months of chemotherapy might be used to improve treatment.

PROTOCOL ENTRY CRITERIA: Patients previously untreated by Radiotherapy and Chemotherapy with histologically proven Stage III or IV epithelial carcinoma of the ovary, who have undergone maximal surgical tumor reduction, accurate staging, and careful documentation of residual disease. Patients must have an estimated survival time of a least 3 months, may not have serious heart disease and must have at least 4000/cumm wbc, 100,000/cumm platelets, BUN not above 30 mg/dl, and creatinine not above 1.5 mg/dl.

PROTOCOL OUTLINE: Randomized study. Enter all patients to Arm I for initial therapy, then treat separately patients with no clinical evidence of disease (NCD), with clinical disease present (CDP) and those with disease progression (PD). For NCD, continue complete responders (CR) on Arm I and randomize partial responders (PR) and patients with no change (NC) to continue Arm I or to enter Arm II. For CDP, randomize patients to continue Arm I or to enter Arm II. Randomize PD receiving L-PAM at any level to Arm III or Arm IV, and cross over patients who continue to fail. Enter PD receiving HAM to Arm III. Remove patients with continued PD from study.

Arm I: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

Arm II: 3-Drug Combination Chemotherapy. HAM: L-PAM; Hexamethylmelamine, HMM, NSC-13875; Adriamycin, ADR, NSC-123127.

Arm III: Single-agent Chemotherapy. Cis-Platinum, CACP, NSC-119875.

Arm IV: 2-Drug Combination Chemotherapy. ADR; HMM.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Partial response rate, complete response rate, time to disease progression, survival time, objective tumor response.

CURRENT STATUS: About 300 patients will be entered.

DOSAGE SCHEDULE:

Arm I: L-PAM - 8.0 mg/sqm/day po on days 1 through 4 q 4 weeks for 6 courses. Escalate drug dosage to 12.0 mg/sqm/day (maximum dose) within 2 courses if hematological toxicity permits. Evaluate all patients after 6 courses. For NCD's perform laparoscopy and then continue CR's on L-PAM for an additional 12 courses or until disease progression; rerandomize PR's and NC's to continue L-PAM for 12 courses or to Arm II. Randomize CDP's to continue Arm I therapy or to enter Arm II; after 12 courses clinically evaluate all CDP's, perform second look laparotomy on CR's and give no further therapy to CR's; continue PR's and NC's on therapy for 4 more years, omitting ADR as indicated. Randomize PD to Arm III or IV with crossover upon further PD.

Arm II: HAM: L-PAM - 4 mg/sqm po on days 1 through 4; HMM - 160 mg/sqm po on days 1 through 14; ADR - 40 mg/sqm (total cumulative dose -480 mg/sqm) iv on day 1. Repeat course q 4 weeks. Give a total of 12 courses of HAM, omitting ADR after maximal dose has been given or if cardiotoxicity occurs, substituting an increase in HMM to 6 mg/kg/day. Perform second look laparotomy on all NCD's and CDP's with CR, then give no further therapy to CR. Continue Arm I or Arm II therapy without ADR for PR and NC patients for 4 years or until disease progression (PD). Enter PD to Arm III.

Arm III: CACP - 50 mg/sqm iv q 28 days.

Arm IV: ADR - 40 mg/sqm on day 1; HMM - 240 mg/sqm po on days 1 through 14 q 28 days.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

4.0051 SURGERY PLUS COMBINATION CHEMOTHERAPY WITH HEXA-CAF AND CHAP-5 FOR STAGE III AND IV OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) DUT-OV-1

OBJECTIVES:

I. Compare (for response, remission, survival, toxicity, and psychological load on the patient) alternating combination chemotherapy CHAP-5 (adriamycin/cis-platinum/cyclophosphamide/hexamethylmelamine) with the standard combination chemotherapy Hexa-CAF (5-fluorouracil/methotrexate/cyclophosphamide/hexamethylmelamine) in patients with ovarian carcinoma Stage III or IV.

II. Determine whether primary maximal surgical debulking followed by chemotherapy gives the patient a better prognosis than does primary chemotherapeutic treatment followed by tumor-reductive surgery.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven epithelial , FIGO Stage III or IV ovarian tumor (serous cystadenocarcinoma, mucinous cystadenocarcinoma, undifferentiated adenocarcinoma). Patients must have a clinical, laparoscopical, or at laparotomy evaluable and measurable tumor parameter. Patients must be under 70 years of age and must have a life expectancy of at least 2 months. They must have had no prior chemotherapy or radiotherapy. There must be no serious cardiac disease nor second malignant disease (except radically treated cervical carcinoma in situ or basal cell skin carcinoma). Staging must be performed within 4 weeks prior to entry. Patient follow-up must be feasible.

PROTOCOL OUTLINE: Randomized study. All patients undergo staging laparotomy, and maximum debulking is performed (as much tumor as possible is removed). The operation is withheld where clinical findings indicate that not all metastases can be removed or reduced. Following Surgery, patients are randomized for Chemotherapy. Patients will undergo restaging laparotomy or laparoscopy at various times between Chemotherapy cycles; in cases where tumor reduction has rendered tumor masses resectable, maximum debulking is performed.

Arm I: 4-Drug Combination Chemotherapy. CHAP-5: Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875; Cyclophosphamide, CTX, NSC-26271; Hexamethylmelamine, HMM, NSC-13875.

Arm II: 4-Drug Combination Chemotherapy. Hexa-CAF: 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740; CTX; HMM.

Maintenance: 2-Drug Combination Chemotherapy. HMM; CTX.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; tumor measurements: echography, CT scan, liver and spleen scintigraphy.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, survival, psychological load on the patient.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CHAP-5: ADR - 35 mg/sqm iv on day 1; CACP - 20 mg/sqm iv over 4 hours with pre- and posthydration on day 1; CTX - 100 mg/sqm po on days 15 through 28; HMM - 150 mg/sqm po on days 15 through 28. No therapy is given during the last week of the cycle. Starting on day 36, the cycle is repeated.

Arm II: Hexa-CAF: MTX - 40 mg/sqm iv on days 1 and 8; 5-FU - 600 mg/sqm iv on days 1 and 8; CTX - 100 mg/sqm po on days 1 through 14; HMM - 150 mg/sqm po on days 1 through 14. No therapy is given on days 15 to 28. Starting on day 29, the cycle is repeated.

Maintenance: CTX - 100 mg/sqm po on days 1 through 14; HMM - 150 mg/sqm po on days 1 through 14.

Patients who initially undergo maximum debulking receive 6 cycles of Arm I or II Chemotherapy. Following 6 cycles of Chemotherapy, restaging laparoscopy or laparotomy is performed. Patients in CR receive 6 more months of Chemotherapy; those in PR receive 6 more cycles of Chemotherapy; those showing no response continue Chemotherapy or proceed to Maintenance. Patients who have large tumor residue (including those with no initial debulking) undergo restaging laparoscopy or laparotomy after 3 or 6 cycles of Arm I or II Chemotherapy. Patients in CR receive 6 more months of Chemotherapy; those showing PR continue Chemotherapy until CR or disease progression. Those showing no change after 6 cycles continue Chemotherapy (on Arm I or II) or change to Maintenance. If patients who received no initial debulking are now eligible for Surgery, tumor debulking is performed and no further treatment given. All patients in CR will undergo laparoscopy after 1 and 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

4.0052 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) EORTC-16792

OBJECTIVES:

I. Define the antitumor activity of m-AMSA in advanced ovarian carcinoma.

PROTOCOL ENTRY CRITERIA: Patients less than 75 years of age with histologically proven serous, mucinous, endometrioid and undifferentiated ovarian FIGO Stage III or IV carcinoma, with measurable disease (pleural effusions, ascites, osseous and CNS metastases are not acceptable as measurable lesions). Patients must have: adequate hematologic, renal and hepatic function; a Karnofsky performance status above 40; and an expected survival of at least 2 months. They must have received no chemotherapy and/or radiotherapy for 3 weeks prior to entry. Patients must not have a second primary malignancy (except treated skin cancer), senility, psychosis, CNS disease, active infection or severe malnutrition.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; chest x-ray; pelvis examination; abdominal circumference.

END POINTS: Response/remission rate, objective tumor response, survival length.

CURRENT STATUS: 14 patients will be entered initially; for each response, additional patients will be entered.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm (90 mg/sqm for patients with extensive prior chemotherapy and/or radiotherapy) iv infusion over 1 hour q 3 weeks. Patients should be treated for a minimum of 2 series; those with progressive disease or unmanageable toxicity go off study; those showing an objective response or stable disease continue treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 10/80

4.0053 L-PAM MAINTENANCE THERAPY WITH OR WITHOUT PRIOR POSTSURGICAL RADIOTHERAPY FOR EPITHELIAL CANCER OF THE OVARY, STAGES IC, IIB, & III

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PROTOCOL NUMBER(S) EORTC-55772

OBJECTIVES:

I. Determine whether abdominal pelvic irradiation added to maintenance chemotherapy with melphalan for epithelial carcinoma of the ovary, Figo Stages IC, IIB, and III will improve remission duration and survival.

PROTOCOL ENTRY CRITERIA: Patients less than 75 years of age with histologically proven epithelial carcinoma of the ovary, including serous, mucinous and clear cell cystadenocarcinoma, endometrioid and undifferentiated adenocarcinoma, Figo Stages IC, IIB, and III with less than 2 cm residual disease. Patients must have a life expectancy of at least 2 months, must have recovered from and be within 2 months of total abdominal hysterectomy plus bilateral salpingoophorectomy with omentectomy and liver biopsies and debulking as indicated. Patients must have minimal counts of 3000 wbc and 150,000 platelets and must not have had prior treatment with radiotherapy or chemotherapy.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arm I or II, then enter all patients to Maintenance Regimen.

Arm I: Radiotherapy. A. Whole abdomen plus pelvic irradiation or B. Moving strip technique.

Arm II: No Radiotherapy. Enter patients directly to Maintenance.

Maintenance Regimen: Single-agent Chemotherapy. Melphalan, L-PAM, NSC-8806.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Liver and renal function tests, SMA-12, IVP, peritoneoscopy (not for Stage III).

END POINTS: Toxicity/morbidity of treatment, time and site of first recurrence, relapse-free interval, duration of survival.

CURRENT STATUS: 152 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: A. 2000 rads given to pelvis in 2 weeks to patients without macroscopic residual disease, or 3000 rads given to pelvis in 3 weeks to patients with macroscopic residual disease, plus 3000 rads given in 4 weeks to the whole abdomen. B. 2600 rads tumor dose given in 12 fractions (8 fractions using direct beam, 4 fractions using penumbra from cobalt) plus 2000 to 3000 rads tumor dose given in 2 to 3 weeks to the pelvis. Liver and kidney shielding is used in both techniques A and B.

Arm II: No Radiotherapy.

Maintenance: Enter patients exiting from Arm I as soon as possible after completion and within 2 months of Radiotherapy. L-PAM - 0.2 mg/kg/day po on days 1 through 5 q 4 weeks for 12 months. Delay therapy if wbc less than 3000 and platelets less than 150,000. Follow up all patients q 3 months for the first 3 years, q 4 months in the 4th year, q 6 months in the 5th year, and once a year after 5 years.

Remove patients with disease progression from study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 04/79

4.0054 SINGLE-AGENT CHEMOTHERAPY WITH BLEOMYCIN FOR OVARIAN CARCINOMA STAGES III AND IV

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PROTOCOL NUMBER(S) EORTC-55775

OBJECTIVES:

I. Determine the therapeutic efficacy of bleomycin for ovarian carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with serous, mucinous, endometrioid, undifferentiated or mesonephrotic ovarian carcinoma with measurable disease at FIGO Stage III or IV. Patients must be less than 65 years of age and must have an expected survival time of over 4 weeks and adequate pulmonary and renal functions.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Bleomycin, BLEO, NSC-125066.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Performance status (Karnofsky); chest x-ray; SMA-12 sonogram or delta scan to assess intraabdominal disease; liver and bone scans.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 20 patients are to be entered.

DOSAGE SCHEDULE:

Administer one course of treatment and follow up patients for 3 months or until disease progresses.

BLEO - 20 mg/sqm continuous iv in 5% dextrose on day 1 through day 7. Examine patients daily for mucositis of the oral cavity and with chest auscultation for the presence of pleural rubs. If these symptoms appear discontinue therapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

4.0055 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) EORTC-55803

OBJECTIVES:

I. Assess the objective antitumor activity of PALA in patients with advanced ovarian cancer previously treated with conventional chemotherapy.

II. Characterize the toxic effects of PALA.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven serous, mucinous, endometrioid, undifferentiated, FIGO Stage III or IV, recurrent ovarian carcinoma. Patients must have measurable disease (pleural effusions, ascites, osseous and CNS metastases not acceptable as measurable lesions). Patients must be under 75 years of age and must have a Karnofsky performance status above 40 and an expected survival of at least 3 months; hematologic, renal, and hepatic functions must be adequate. Patients must have no second primary malignancy (except treated skin cancer), senility, psychosis, CNS disease, active infection, or severe malnutrition; they must receive no chemotherapy or radiotherapy for at least 3 weeks prior to entry (6 weeks for nitrosoureas or extensive radiotherapy).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; chest x-ray; pelvic examination; abdominal circumference.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: Initially 14 patients will be entered. On the basis of the response observed in these 14, additional patients will be entered.

DOSAGE SCHEDULE:

PALA - 2.5 g/sqm/day iv for 2 days q 2 weeks (i.e., days 1, 2, 15, 16) if toxicity has abated. Patients showing regression continue treatment until tumor progression; those showing no change stop treatment after 6 courses. Patients showing progression after 3 courses go off treatment. Treatment is discontinued whenever severe toxicity is encountered.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 1 g ampules.

DATE SUMMARIZED: 10/80

4.0056 CHEMOTHERAPY WITH CHLORAMBUCIL VS CHLORAMBUCIL PLUS HORMONE THERAPY WITH PROGESTIN FOR STAGES III AND IV ADVANCED OVARIAN CARCINOMA

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PROTOCOL NUMBER(S) UICC-76034; ITA-BOL-171O

OBJECTIVES:

I. Compare Phase III multimodality therapy with chlorambucil plus medroxyprogesterone acetate (MPA) vs. single-agent chemotherapy with chlorambucil for advanced carcinoma of the ovary stage III, stage IV or with local recurrence.

II. Evaluate the prognostic significance of some stratification factors in these two regimens.

PROTOCOL ENTRY CRITERIA: Patients with measurable lesions of ovarian carcinoma, stage III, stage IV (Figo classification), locally recurrent with clear evidence of progression with or without metastases. Patients must be between 30 and 70 years of age, have a performance status greater than 40 and have an estimated survival time of 2 months or more. Wbc must be at least 4500 and platelet count at least 80,000.

PROTOCOL OUTLINE: Randomized study.

Induction and Maintenance:

Arm I: Single-agent Chemotherapy. Chlorambucil, CLB, NSC-3088.

Arm II: Single-agent Chemotherapy plus Hormone Therapy. CLB; plus Medroxyprogesterone acetate, MPA, NSC-26386.

STRATIFICATION BY: Disease stage: III, IV or recurrent; participating institutions; age (30-39, 40-49, 50-59, 60-70); prior therapy; histologic type.

SPECIAL STUDY PARAMETERS: EKG, barium enema, IVP.

END POINTS: Response/recurrence rate, disease progression, survival rate, toxicity/morbidity of treatment, duration of survival, objective tumor response.

CURRENT STATUS: 48 patients to be entered.

DOSAGE SCHEDULE:

Arm I: Induction: CLB - 0.20 mg/kg (route not given) daily for 25 days followed by a rest period of 60 days. Maintenance: CLB - 0.20 mg/kg daily on days 1 through 5 q month.

Arm II: Induction: CLB - as in Arm I; MPA - 1500 mg daily for thirty days followed by a rest period of 60 days. Maintenance: CLB - as in Arm I, MPA - 1000 mg/day twice a week.

Follow patients q 2 months until disease progression or death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 01/77

4.0057 ADJUVANT CHEMOTHERAPY WITH CLB OR HMM FOR EARLY OVARIAN CANCER

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PROTOCOL NUMBER(S) UICC-76077

OBJECTIVES:

I. Determine the therapeutic efficacy of single-agent chemotherapy with either chlorambucil or hexamethylmelamine for early ovarian cancer following apparent complete excision.

PROTOCOL ENTRY CRITERIA: Patients who have undergone surgery with apparently completely excised localized ovarian cancer without evidence of extension of the tumor through the capsule or significant adhesion of the capsule to other structures. Includes FIGO classification Stages IA and B.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Chlorambucil, CLB, NSC-3088.

Arm II: Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

Arm III: Control Group. No treatment.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Optional blood markers; annual chest x-ray; exploration and biopsy of suspected lesions.

END POINTS: Relapse/recurrence rate, toxicity/morbidity of treatment, survival rate, duration of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Begin supplemental therapy within 2 to 4 weeks after surgery.

Arm I: CLB - 10 mg/day po on days 1 through 14 followed by 14 days without treatment. Repeat for 7 courses during 6 months.

Arm II: HMM - 400 mg/day po on days 2 through 14 followed by 14 days without treatment. Repeat for 7 courses during 6 months.

Arm III: Control group. No treatment. Follow up patients for 5 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/77

4.0058 CHEMOTHERAPY WITH CTX/ADR/HEXAMETHYLMELAMINE VS CTX/ADR/CIS-PLATINUM FOR EPITHELIAL OVARIAN CANCER STAGES III AND IV

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PROTOCOL NUMBER(S) UICC-78026

OBJECTIVES:

I. Study and compare treatment with cyclophosphamide (CTX)/adriamycin (ADR)/hexamethylmelamine vs. CTX/ADR/cis-platinum for Stages III and IV ovarian cancer with respect to number and degree of responses, length of responses and toxicity vs. benefits.

PROTOCOL ENTRY CRITERIA: Patients less than 70 years of age with a histological diagnosis of Stage III or IV epithelial ovarian cancer including serous, mucinous, undifferentiated, endometrioid, mesonephroid and malignant Brenner tumors. Patients must not have had prior chemotherapy, radiotherapy or curative surgery without residual disease. They must have an expected survival of at least 3 months, and normal bone marrow, hepatic, renal and cardiac function.

PROTOCOL OUTLINE: Randomized study. Randomize patients following staging work up 10 days after surgery. All responders proceed to Maintenance.

Arm I: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Hexamethylmelamine, HMM, NSC-13875.

Arm II: 3-Drug Combination Chemotherapy. CTX; ADR; plus cis-Platinum, CACP, NSC-119875.

Maintenance: Single-agent Chemotherapy. CACP.

STRATIFICATION BY: Residual tumor size: 2 cm or less vs. over 2 cm.

SPECIAL STUDY PARAMETERS: Liver scan, urography, lymphangiogram, phonocardiography, audiometry and (where indicated) barium enema, laparoscopy, laparotomy, colonoscopy and ultrasound.

END POINTS: Response/remission rate, response duration, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULES:

Arm I: CTX - 70 mg/sqm/day po on days 1 through 14; ADR - 50 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on day 1; HMM - 150 mg/sqm po on days 1 through 14. Repeat courses q 4 weeks for a maximum of 9 courses.

Arm II: CACP - 50 mg/sqm iv on day 1 with adequate hydration and mannitol diuresis; ADR and CTX, as in Arm I except give CTX iv. Repeat course q 4 weeks for a maximum of 9 courses.

Evaluate all patients after 3 months of therapy. Remove nonresponders (NR) and patients without change (NC) from study. Perform laparoscopy for complete (CR) or partial responders (PR) and if tumor response is not otherwise evaluable. Enter all responders to Maintenance.

Maintenance.

CTX - 70 mg/sqm/day po. Evaluate patients after 9 months of Maintenance. Remove patients with DP or NC from study. Follow up responders with NED without further treatment; if clinical possibility of NED after surgical resection, perform laparoscopy and/or second look laparotomy. Perform laparotomy on patients with NED or laparoscopy at 18 months. Continue Maintenance therapy and re-evaluate after 6 months patients with NED after curative resection and patients with microscopic disease or with cytologically positive washing at surgery.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; CTX - 100 mg vials and 50 mg capsules; CACP - 10 mg vials; HMM - 100 mg capsules.

DATE SUMMARIZED: 07/79

4.0059 IMMUNOTHERAPY WITH NON-IMMUNE OR TUMOR-IMMUNE PIG LYMPH NODE CELLS FOR CARCINOMA OF THE OVARY

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PROTOCOL NUMBER(S) UKM-OV-1

OBJECTIVES:

I. Compare the antitumor action of non-immune and tumor-immune pig lymph node cells in patients with carcinoma of the ovary.

PROTOCOL ENTRY CRITERIA: Patients over 21 years of age with carcinoma of the ovary who have previously received surgery and/or radiotherapy and/or cytotoxic chemotherapy to the maximum permitted level. Patients must have ascites confirmed by laparoscopy and biopsy that are associated with recurrent intra-abdominal tumor. Metastases must be accessible to a regional injection of lymph node cells.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. Non-immune pig lymph node cells.

Arm II: Immunotherapy. Tumor-immune pig lymph node cells.

STRATIFICTION BY: None given.

SPECIAL STUDY PARAMETERS: Physical examination, sonar studies of the abdominal cavity, laparoscopy, laparoscopic biopsy, tumor measurements.

END POINTS: Response/remission rate, length of remission, length of survival.

CURRENT STATUS: 30 patients per year will be entered over a 3-year period.

DOSAGE SCHEDULE:

Arm I: Non-immune pig lymph node cells - 1.0 x 10 to the 9th viable cells ip via a paracentesis needle after the withdrawal of as much ascitic fluid as possible, and 1.5 x 10 to the 9th viable cells injected via a transfemoral Seldinger catheter into the arterial blood supply of the main intraperitoneal tumor mass.

Arm II: Tumor-immune pig lymph node cells - 1.0 x 10 to the 9th viable cells ip as per Arm I and 1.5 x 10 to the 9th viable cells injected via a transfemoral Seldinger catheter as per Arm I. Patients receive a single treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 08/80

4C. UTERUS

4.0060 PROPHYLACTIC CHEMOTHERAPY WITH ADRIAMYCIN ADJUVANT TO SURGERY AND RADIOTHERAPY FOR STAGE I AND STAGE II UTERINE SARCOMAS

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) GOG-20

OBJECTIVES:

I. Determine the efficacy of adjuvant chemotherapy with adriamycin for stage I and stage II uterine sarcomas.

PROTOCOL ENTRY CRITERIA: Stage I and stage II sarcomas of the uterine corpus with no gross residual disease following surgery. Prior to randomization patients will have had a total abdominal hysterectomy with bilateral salpingo-oophorectomy with or without pre- or post-operative radiotherapy. Patients will be entered 1 to 4 weeks post surgery or post radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I. Control.

Arm II: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions; radiotherapy or no radiotherapy; histologic type: leiomyosarcoma, endometrial stromal sarcoma, carcinosarcoma, malignant mixed mullerian tumor, other uterine sarcomas.

SPECIAL STUDY PARAMETERS: IVP.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, duration of response, disease-free interval.

CURRENT STATUS: 180 patients to be entered.

DOSAGE SCHEDULE:

Arm I. Control.

Arm II: Single-agent Chemotherapy. ADR - 60 mg/sqm iv as a single dose q 3 weeks for 24 weeks. Monitor wbc and platelets q 3 weeks and IVP q 6 weeks. Follow patients q 3 months for 2 years and q 6 months thereafter or until recurrent disease.

Dosage modifications for toxicity are given. Patients who exit from Protocol GOG-20 may be treated with the VAC regimen (Amendment July 1975) as follows: Vincristine - 1.5 mg/sqm iv (maximum single dose 2.5 mg) q week for 8 to 12 weeks; plus Actinomycin-D - 0.5 mg iv q day on days 1 through 5; plus Cyclophosphamide - 7 mg/kg q day on days 1 through 5.

DOSAGE FORMS: ADR - 10 mg and 20 mg vials.

DATE SUMMARIZED: 01/77

PATIENT ACCRUAL: 01520179

4.0061 CHEMOTHERAPY WITH ADRIAMYCIN FOLLOWING SURGERY AND RADIOTHERAPY FOR ENDOMETRIAL CARCINOMA, STAGE I AND OCCULT STAGE II

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PROTOCOL NUMBER(S) GOG-7743; GOG-34

OBJECTIVES:

I. Compare differences in morbidity and patient survival as functions of various tumor growth patterns as well as treatment with surgery, radiotherapy and chemotherapy with adriamycin (ADR) for high risk Stage I and, optionally, high risk occult Stage II endometrial carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with primary, previously untreated, histologically confirmed invasive carcinoma of the endometrium Stage I and occult Stage II, all grades. Patients must have either adenocarcinoma, adenocanthoma, or adenosquamous carcinoma with lesions of at least one half myometrial involvement, positive pelvic and/or para-aortic nodes, or microscopic evidence of cervical involvement without gross clinical involvement. Patients must not have had previous pelvic irradiation or chemotherapy, and must have adequate hematologic status. Patients will undergo exploratory laparotomy; those with disease beyond the uterus, cervix, and adnexa, other than those with pelvic and/or para-aortic nodal involvement, will be excluded. (Patients with adnexal metastases are eligible. Addendum, October 1979.)

PROTOCOL OUTLINE: Randomized study. Enter all patients in Surgery, Regimen A, then randomize to Arms I and II prior to Radiotherapy (Revision, December 1978).

Regimen A: Surgery plus Radiotherapy: Megavoltage - 1 MeV or Cobalt-60.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: No further treatment.

STRATIFICATION BY: Participating institutions, 4 categories of involvement of para-aortic and pelvic nodes and cervix.

SPECIAL STUDY PARAMETERS: Renal and hepatic function tests, peritoneal cytology, IVP, EKG, D and C.

END POINTS: Response/remission rate, survival rate, progression-free interval, GOG Performance Status, toxicity/morbidity of treatment, frequency and duration of partial responses, survival time, incidence of spread to pelvic and para-aortic nodes.

CURRENT STATUS: 270 patients will be entered in about 4 years.

DOSAGE SCHEDULE:

Regimen A: Total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic lymphadenectomy with lymph node sampling. Radiotherapy - for patients with negative para-aortic nodes: 5000 rad delivered homogeneously to the pelvis in 5 to 6 weeks beginning 2 to 6 weeks after surgery. For patients with positive para-aortic nodes: 4500 rad para-aortic dose plus 5000 rad external pelvic dose. If biopsy positive, use Pan-Handle technique.

Arm I: Begin within 2-4 weeks of radiation therapy. ADR - 45 mg/sqm iv q 3 weeks. Add 15 mg/sqm with each successive course to reach 90 mg/sqm. (Maximum cumulative dose 400 mg/sqm).

Arm II: No further treatment.

Follow up patients every 3 months for 3 years, then every 6 months for 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00260179

4.0062 PHASE III ADRIAMYCIN CHEMOTHERAPY WITH OR WITHOUT CYCLOPHOSPHAMIDE FOR RECURRENT OR ADVANCED UTERINE SARCOMA

Lewis, C. G., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) GOG-7842; GOG-42

OBJECTIVES:

I. Determine if Adriamycin alone is more effective than Adriamycin and Cyclophosphamide in producing response in advanced or recurrent uterine sarcoma.

II. Determine the duration of response for each different treatment arm.

PROTOCOL ENTRY CRITERIA: Patients with any cell type of histologically confirmed recurrent or Stage III or Primary Stage IV uterine sarcoma, who have completed radiotherapy to the pelvic bed, if given, more than 3 months prior to study entry. Patients must have a GOG performance status of 0 to 3, must have adequate bone marrow, renal, hepatic and cardiac functions, and must not have had prior chemotherapy for their disease. Pretreatment granulocyte count must be at least 2000/cumm (Addendum July 1979).

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: 2-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; plus ADR.

STRATIFICATION BY: Performance Status: 0 or 1 vs. 2 or 3; prior radiotherapy.

SPECIAL STUDY PARAMETERS: Abdominal CAT, ultrasound of pelvis and para-aortic nodes, IVP, lung tomograph.

END POINTS: Objective tumor response, response/remission rate, survival, progression-free interval, toxicity/morbidity of treatment.

CURRENT STATUS: 150 patients will be entered in about 5 years.

DOSAGE SCHEDULE:

Enter patients following surgery and maximum tumor removal.

Arm I: ADR - 60 mg/sqm iv q 3 weeks. Discontinue therapy when cumulative dosage has reached 480 mg/sqm.

Arm II: CTX - 500 mg/sqm iv q 3 weeks; plus ADR as in Arm I.

Remove from study patients who have received the maximum ADR therapy and patients with disease progression. Follow up all patients for life.

Dosage modifications for toxicity, poor-risk patients, and patients with hepatic dysfunction are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200 and 500 mg vials.

DATE SUMMARIZED: 06/79

4.0063 PHASE III PROVERA (MPA) HORMONAL THERAPY VS ADR VS ADR/CTX FOR PRIMARY STAGE III OR IV RECURRENT OR RESIDUAL ENDOMETRIAL CANCER

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PROTOCOL NUMBER(S) GOG-7941; GOG-48

OBJECTIVES:

I. Evaluate the response of advanced or recurrent endometrial carcinoma to oral progestins in patients who have received no prior hormonal therapy.

II. Compare combination chemotherapy with adriamycin (ADR)/cyclophosphamide (CTX) vs. ADR alone for advanced or recurrent endometrial carcinoma which no longer responds or has failed to respond to progestins in patients who have received no prior cytotoxic drugs.

III. Confirm the reported 37% response rate of advanced or recurrent endometrial carcinoma to ADR.

IV. Confirm the survival benefit in responders to cytotoxic drugs.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed FIGO stage III or IV concurrent or residual endometrial adenocarcinoma, adenoacanthoma or adenosquamous carcinoma (whose potential for cure by radiotherapy or surgery alone or in combination is very poor. Addendum, January 1980). Patients must have a minimum life expectancy of 1 month, a GOG performance status of 3 or better, adequate cardiac, hematologic, renal and liver function and no prior chemotherapy.

PROTOCOL OUTLINE: Randomized study. Enter patients with no prior hormone therapy to Arm I. Randomize all others to Arm II or III 3 weeks after completion of prior hormone therapy.

Arm I: Hormone Therapy. Medroxyprogesterone acetate (Provera), MPA, NSC-26386.

Arm II: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm III: 2-Drug Combination Chemotherapy. ADR; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION: Participating institutions; performance status: 0-1 vs. 2-3; prior radiotherapy; site of disease; pelvic vs. extrapelvic.

SPECIAL STUDY PARAMETERS: Hepatic and renal function.

END POINTS: Response/remission rate, relapse rate, survival time, duration of response, toxicity/morbitity of treatment.

CURRENT STATUS: 300 patients will be entered in 2.5 to 3 years.

DOSAGE SCHEDULE:

Arm I: MPA - 150 mg/day po for at least 12 weeks. Continue therapy until disease progression, then randomize patients into Arm II or III.

Arm II: ADR - 60 mg/sqm (maximum cumulative dose 480 mg/sqm) iv on day 1 q 3 weeks for 8 courses.

Arm III: ADR as in Arm I; CTX - 500 mg/sqm iv on day 1 q 3 weeks for 8 courses. Remove patients with disease progression or upon reaching maximum cumulative ADR dose. Follow all patients q 3 months until death.

Dosage modifications for poor risk patients, hepatic dysfunction and for toxicity are given.

DOSAGE FORMS: ADR - 10 mg and 50 mg vials; CTX - 100, 200 and 500 mg vials; MPA - 50 mg tab.

DATE SUMMARIZED: 04/80

4.0064 INTRACAVITARY IRRADIATION AND EXTERNAL IRRADIATION ALONE OR COMBINED, PRIOR TO TAH-BSO FOR ENDOMETRIAL CARCINOMA

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PROTOCOL NUMBER(S) RTOG-7926

OBJECTIVES:

I. Compare external beam irradiation to the pelvis vs. external beam irradiation plus intracavitary radiation vs. intracavitary radiation, each followed by total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) for Stage I, Grade II-III endometrial carcinoma with respect to the frequency of vaginal and/or pelvic recurrence, survival, long-term or delayed complications related to normal pelvic structures, and surgical and/or surgical-pathologic findings.

PROTOCOL ENTRY CRITERIA: Patients with operable FIGO Stage IA, biopsy-proven endometrial adenocarcinoma with uterine sounding of under 8 cm and histologic Grade III or patients with operable Stage IB with a uterine sounding of 8 cm or more and histologic Grade II or III. Patients must be under 75 years of age and have a life expectancy of at least 5 years.

PROTOCOL OUTLINE: Study randomized within the Radiotherapy regimen.

Regimen A: Radiotherapy.

Arm I: Intracavitary Irradiation. Two insertions of radium, cesium, or another suitable isotope.

Arm II: External Irradiation plus Intracavitary Irradiation. Co-60 or higher energy megavoltage external irradiation to the pelvis followed by intracavitary packing.

Arm III: External Irradiation. Megavoltage irradiation as in Arm II.

Regimen B: Surgery. TAH and BSO 4-6 weeks after the completion of radiotherapy.

STRATIFICATION BY: Participating institutions, histologic grade, tumor stage.

SPECIAL STUDY PARAMETERS: Pelvic examinations, biopsies as indicated, chest film, BUN/creatinine, IVP as indicated, barium enema as indicated.

END POINTS: Recurrence rate, survival, delayed complications of therapy, surgical and/or surgical-pathologic findings.

CURRENT STATUS: 150 patients are anticipated in each arm over a 4-year period.

DOSAGE SCHEDULE:

Regimen A: Radiotherapy.

Arm I: Two insertions of radium, cesium, or another similar isotope, separated by 2-3 weeks; total uterine dose 5000 mg hours; upper vaginal surface should receive 7000-8000 rad in 2 applications.

Arm II: Co-60 megavoltage, preferably with an AP/PA 2 field portal arrangement, 180-200 rad/day, 5 fractions/week (treating all fields daily), to dose of 4000 rad in 32 days. Intracavitary radiation: uterus, 2500 mg hours; vagina, 3000-4000 rad surface dose.

Arm III: Co-60 as in Arm II, 180-200 rad/day, 5 fractions/week to a dose of 4500-5000 rad in 5-5.5 weeks.

-Regimen B: Extrafascial TAH and BSO with exploration for nodal and extra-pelvic spread, including biopsy of suspicious nodes and pelvic fluid cytology, 4-6 weeks after completion of Radiotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 06/80

4.0065 PHASE II STUDY OF CACP VS ADR/CTX/CACP FOR STAGE III-IV ENDOMETRIAL CARCINOMA

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PROTOCOL NUMBER(S) MAYO-796052; NCCTG-796052

OBJECTIVES:

I. Compare the efficacy of cis-platinum as a single agent with that of cis-platinum/cyclophosphamide/adriamycin in the treatment of advanced endometrial adenocarcinoma.

II. Assess the efficacy of the sequential use of cyclophosphamide/adriamycin in patients following cis-platinum therapy in this study.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage III-IV carcinoma of the uterine corpus not amenable to surgical or radiotherapeutic treatment. Patients must have evaluable disease and must demonstrate clearly progressive disease if they have received hormonal therapy prior to entry; they must not be candidates for other hormonal therapy. The ECOG performance score must be 3 or better and expected survival must be greater than 2 months. Patients may not have had another primary malignancy within 5 years (except curable skin cancer) and may not have a history of active heart disease. Liver and kidney function must be adequate. Patients may not have received prior treatment with any of the protocol agents.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; CACP.

STRATIFICATION BY: Performance score (0-1 vs. 2-3), histologic grade (1-2 vs. 3-4), disease stage (III vs. IV).

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic parameters, chest x-ray, EKG.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: Fifteen patients per year will be accrued over a 2-year period.

DOSAGE SCHEDULE:

Arm I: CACP - 60 mg/sqm iv infusion with concomitant forced diuresis. Repeat course at 21-28 days. Continue therapy until progression, at which time stop CACP and treat with CTX (500 mg/sqm iv) plus ADR (40 mg/sqm iv), repeating cycles q 21-28 days. For patients with prior pelvic external radiation of greater than 3500 rads, the doses of CTX and ADR should be 400 and 30 mg/sqm, respectively. Continue until progression, upon which patients go off study.

Arm II: CTX - 400 mg/sqm iv; ADR - 40 mg/sqm iv (maximum cumulative dose 500 mg/sqm); CACP - 40 mg/sqm iv infusion with concomitant forced diuresis. For patients with greater than 3500 rads prior pelvic external irradiation the doses, of CTX, ADR, and CACP will be, respectively, 300, 30, and 30 mg/sqm. Repeat courses q 28 days. Continue therapy until progressive disease. After maximum allowable dose of ADR has been given, continue treatment with CTX and CACP until progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; ADR - 10 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 07/80

4.0066 CAF (CTX/ADR/5-FU) WITH OR WITHOUT HORMONE SYNCHRONIZATION WITH MEG AND PREMARIN FOR ADVANCED ENDOMETRIAL ADENOCARCINOMA

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PROTOCOL NUMBER(S) NCI-79-C-72; NCI-MB-125

OBJECTIVES:

I. Compare CAFFI (4-day infusion of 5-fluorouracil and adriamycin with pulse cyclophosphamide) vs. conventional CAF (cyclophosphamide/adriamycin/5-fluorouracil) in patients with advanced endometrial adenocarcinoma who have failed prior progesterone therapy.

II. Study the pharmacokinetics of continuous infusions as given in CAFFI.

III. Study the effectiveness of CAFFI in combination with suppressive and stimulatory hormone treatment using megestrol acetate and Premarin.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven endometrial adenocarcinoma who have objective evidence of measurable tumor recurrence that cannot be controlled by local therapy. There must be no history of prior chemotherapy, but patients may have failed on prior hormone treatment or they may have had no prior hormone therapy. Bone marrow, liver, and kidney function must be adequate. Patients should be under the age of 70 and must have a performance status of 2 or better and a life expectancy of at least 2 months. There may be no history of ischemic heart disease, cardiomyopathy, congestive heart failure, or colitis.

PROTOCOL OUTLINE: Patients who have failed prior hormone therapy are randomized to Arms I and II. Patients with no prior hormone therapy enter Regimen A.

Arm I: 3-Drug Combination Chemotherapy. CAF: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 3-Drug Combination Chemotherapy. CAFFI: CTX; ADR; 5-FU, administered by continuous infusion.

Regimen A: 3-Drug Combination Chemotherapy plus Hormone Therapy. CAFFI; plus Megestrol acetate, MEG, NSC-71423; Premarin (conjugated estrogens), no NSC number.

STRATIFICATION BY: Disease-free interval (greater vs. less than 1 year), performance status (0-1 vs. 2-4), sites of recurrent or metastatic disease (pelvic or retroperitoneal with or without extrapelvic vs. extrapelvic only).

SPECIAL STUDY PARAMETERS: Chest x-ray, IVP, barium enema, liver/spleen scan, bone scan, hemogram, coagulation studies, chemistries panel, creatinine clearance, indocyanin green clearance, EKG and radionuclide scan, CEA, performance status, lymphangiogram.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: About 35-40 patients will be entered.

DOSAGE SCHEDULE:

Arm I: CAF: 5-FU - 500 mg/sqm iv push on days 1 and 8; ADR - 30 mg/sqm iv over 10 minutes on days 1 and 8 after 5-FU; CTX - 400 mg/sqm iv over 10 minutes on days 1 and 8 after ADR. Repeat cycles q 28 days. Maximum cumulative dose of ADR not to exceed 525 mg/sqm, after which 5-FU and CTX only are given. In the absence of toxicity, escalate 5-FU by 100 mg/sqm/cycle. After stabilization of 5-FU dose, escalate CTX by 100 mg/sqm/cycle.

Arm II: CAFFI: 5-FU - 20 mg/kg/day by continuous iv infusion over days 1 through 4; ADR - 15 mg/sqm/day by continuous iv infusion over days 1 through 4; CTX - 500 mg/sqm/day iv over 10 minutes at the end of day 2 and the end of day 4. Escalate 5-FU by 5 mg/kg/day each cycle until toxicity. Repeat q 28 days.

Regimen A: CAFFI as in Arm II beginning on day 25; MEG - 160 mg/day po in 2 divided doses on days 1 through 22; Premarin - 0.625 mg po q 12 hours for 4 doses beginning on the morning of day 23.

Treat for at least 2 cycles before declaring failure. Patients with progressive disease after 2 cycles go off study. Patients with PR or stable disease continue therapy indefinitely. Patients with CR continue treatment for 4 cycles beyond achievement of CR.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

4.0067 CLINICAL TRIAL OF TAMOXIFEN IN THE TREATMENT OF ADVANCED ENDOMETRIAL CARCINOMA

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PROTOCOL NUMBER(S) NCCTG-796051; MAYO-796051

OBJECTIVES:

I. Assess the efficacy of tamoxifen in the treatment of patients with Stage III/IV endometrial carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with evaluable histologically proven Stage III/IV endometrial carcinoma that is not amenable to surgery or radiotherapy. Patients may not have been treated with tamoxifen in the past, and they must demonstrate clearly progressive disease if they have been treated with any other hormone prior to entry. The ECOG performance score must be 3 or better and the expected survival must be greater than 2 months. There may not have been a known second primary malignancy other than nonmelanomatous skin cancer within 5 years of entry.

PROTOCOL OUTLINE: Nonrandomized study.

Endocrine Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: Performance status (0-1 vs. 2-3), estrogen receptor (positive vs. negative), prior hormonal therapy, prior chemotherapy, site of metastasis (pulmonary vs. pelvic-abdominal vs. other), grade of tumor.

SPECIAL STUDY PARAMETERS: Tumor measurements, hemogram, blood chemistries, chest x-rays.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: About 30 patients are expected to be entered.

DOSAGE SCHEDULE:

TMX - 20 mg/day po in 2 divided doses. Continue stable and improved patients until disease progresses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - 10 mg tablets.

DATE SUMMARIZED: 08/80

4.0068 HORMONAL TREATMENT OF ENDOMETRIAL ADENOCARCINOMA WITH MEDROXYPROGESTERONE ACETATE

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PROTOCOL NUMBER(S) BRA-5837/DTP-ACE-1

OBJECTIVES:

I. Determine the effectiveness of medroxyprogesterone acetate (MAP) in the treatment of adenocarcinoma of the endometrium in terms of therapeutic response and duration of remission.

II. Evaluate tolerance to the treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed endometrial adenocarcinoma. Include Stages III and V (T3 and T4 by the TNM classification). Recurrent or residual disease inaccessible to control by surgery or irradiation alone. Objective evidence of progressive disease and survival prognosis of more than 3 months. Lesion accessible to evaluation by direct measurement or by photography or radiography. Patients must have a performance status of Class 3 or better (Gynecology Oncology Group Grade), without prior treatment with progestational agents, severe cardiovascular disease or CNS involvement.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Hormone Therapy. Medroxyprogesterone acetate, MAP, NSC-26386.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Toxicity/morbidity of treatment, recurrence rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: MAP - 500 mg im twice weekly for 3 months, after which if response satisfactory, 500 mg im weekly for indeterminate period at discretion of investigator.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

4D. GYNECOLOGIC—GENERAL

4.0069 PILOT COMBINATION CHEMOTHERAPY WITH BLEOMYCIN/CIS-PLATINUM PLUS RADIOTHERAPY FOR ADVANCED VAGINAL OR VULVAR CARCINOMA

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Group, 905 University Ave., Suite 415, Madison, Wisconsin,
53715, United States of America
PROTOCOL NUMBER(S) EST-PE-879

OBJECTIVES:

I. Evaluate the toxicity and effectiveness of bleomycin and cis-platinum combined with intensive radiation therapy in patients with advanced inoperable vulvar or vaginal carcinoma.

PROTOCOL ENTRY CRITERIA: Patients of all ages with histologic diagnosis of squamous carcinoma of the vulva or vagina. The disease must be extensive, with clinical or LAG involvement of groin lymph nodes, periurethral tissue or perianal tissue; a gynecologic surgeon must signify that the tumor is beyond hope of surgical cure. The disease must be measurable, and there must be no active second malignancy. There must be adequate renal, bone marrow, and hepatic function. The life expectancy must be more than 3 months, and the performance status 2 or better. There must be no unresolved acute intercurrent medical or psychiatric condition or distant metastases, and the patient must be able to tolerate an intravenous fluid stress.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy plus Radiotherapy. Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875; plus 6 MeV linear accelerator radiation to primary tumor and lymph nodes and boost dose by Iridium-192 implant.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: IVP, bone scan, liver scan, EKG, audiogram, arterial blood gases.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 20 patients will be entered over 2.5-3 years.

DOSAGE SCHEDULE:

CACP - 50 mg/sqm iv push, with adequate hydration with furosemide and mannitol, on days 1 and 22. BLEO - 15 units/sqm iv push on day 3 followed immediately by continuous infusion of BLEO - 15 units/sqm/day for 5 days. Radiotherapy given with 6 MeV linear accelerator will begin on day 23 or 24. Initial therapy to primary - 4500 rads in fractions of 180 rads/day using AP-PA to pelvis. Boost therapy - 6000 rads (180 rads/day) to positive lymph nodes (if present at initial staging), 2000 rads to primary if tumor volume inadequately reduced, 2500-3000 rads by Iridium-192 implant to primary tumor if adequately reduced.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 unit ampules; CACP - 10 mg vials.

DATE SUMMARIZED: 10/80

4.0070 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR ADVANCED GYNECOLOGIC MALIGNANCIES

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234
Market Street, Suite 430, Philadelphia, Pennsylvania, 19107,
United States of America
PROTOCOL NUMBER(S) GOG-26C

OBJECTIVES:

I. Determine the efficacy of cis-platinum for the treatment of patients whose advanced pelvic malignancies have been resistant to high-priority methods of treatment.

PROTOCOL ENTRY CRITERIA: Patients with advanced, recurrent, persistent, metastatic or local gynecologic cancer with documented disease progression and measurable parameters of disease activity who are not eligible for higher priority protocols. Patients must have a GOG performance status of grade 0, 1 or 2, must be free of significant infection, recovered from the effects of recent surgery, radiotherapy or chemotherapy, and be off chemotherapy for at least 3 weeks prior to entry. Patients must have had no prior exposure to the agents under study, and must have no other malignancy, either prior or concomitant, other than skin (excluding melanoma). Wbc of greater than 1500/cumm, platelets of greater than 100,000/cumm, BUN of less than 25 mg%, creatinine of less than 1.5 mg%, bilirubin less than 1.0 mg and SGOT less than 50 IU are required. (Protocol closed to patients with squamous cell carcinoma of the cervix and epithelial ovarian carcinoma in November 1977 and to those with non-squamous cell carcinoma of the cervix and endometrioid carcinoma in November 1979.)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions, disease site.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, progression-free interval, objective tumor response, survival rate, length of survival, toxicity/morbidity of treatment, severity of symptoms and performance status.

CURRENT STATUS: 25 evaluable patients per disease site will be accrued.

DOSAGE SCHEDULE:

CACP - 50 mg/sqm iv infusion. Repeat q 3 weeks, bone marrow, kidney and hearing tolerance permitting. Continue therapy until evidence of disease progression or adverse effects. (Optional method of hydration for out-patient cases given in Amendment, October 1977).

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00980179

4.0071 PHASE II CHEMOTHERAPY WITH VP-16 FOR ADVANCED GYNECOLOGIC MALIGNANCIES

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Market Street, Suite 430, Philadelphia, Pennsylvania, 19107,
United States of America
PROTOCOL NUMBER(S) GOG-26D

OBJECTIVES:

I. Determine the efficacy of VP-16 for the treatment of patients whose advanced pelvic malignancies have been resistant to higher priority methods of treatment.

PROTOCOL ENTRY CRITERIA: Patients with advanced, recurrent, persistent, metastatic or local gynecologic cancer with documented disease progression and measurable parameters of disease activity who are not eligible for higher priority protocols. Patients must have a GOG performance status of grade 0, 1 or 2, must be free of significant infection, recovered from the effects of recent surgery, radiotherapy or chemotherapy, and be off chemotherapy for at least 3 weeks prior to entry. Patients must have had no prior exposure to the agent under study, and must have no other malignancy, either prior or concomitant, other than skin (excluding melanoma). Wbc of greater than 1500/cumm, platelets of greater than 100,000/cumm, BUN of less than 25 mg%, creatinine of less than 1.5 mg%, bilirubin less than 1.0 mg, and SGOT less than 50 IU, are required. For patients with prior therapy with Adriamycin and/or any alkylating agents a granulocyte count above 2,000 and a platelet count above 150,000 are required. (Protocol closed to patients with squamous cell carcinoma of the cervix in January 1978, with epithelial ovarian carcinoma in April 1978,and with non-squamous cell carcinoma of the cervix in November 1979.)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. VP-16, NSC-141540.

STRATIFICATION BY: Participating institutions, disease site.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, progression-free interval, objective tumor response, survival rate, length of survival, toxicity/morbidity of treatment, severity of symptoms and performance status.

CURRENT STATUS: 25 evaluable patients per disease site will be accrued.

DOSAGE SCHEDULE:

VP-16 - 100 mg/sqm iv on days 1, 3 and 5. Repeat q 28 days, bone marrow recovery permitting. Continue therapy until evidence of disease progression or adverse effects.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VP-16 - 100 mg ampules.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00940179

4.0072 PHASE II CHEMOTHERAPY WITH DIANHYDROGALACTITOL FOR ADVANCED GYNECOLOGIC MALIGNANCIES

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) GOG-26E

OBJECTIVES:

I. Determine the efficacy of dianhydrogalactitol for the treatment of patients whose advanced pelvic malignancies have been resistant to high-priority methods of treatment.

PROTOCOL ENTRY CRITERIA: Patients with advanced, recurrent, persistent, metastatic or local gynecologic cancer with documented disease progression and measurable parameters of disease activity, who are not eligible for higher priority protocols. Patients must have a GOG performance status of grade 0, 1 or 2, must be free of significant infection, recovered from the effects of recent surgery, radiotherapy or chemotherapy, and be off chemotherapy for at least 3 weeks prior to entry. Patients must have had no prior exposure to the agent under study, and must have no other malignancy, either prior or concomitant, other than skin (excluding melanoma). Wbc of greater than 1500/cumm, platelets of greater than 100,000/cumm, BUN of less than 25 mg%, creatinine of less than 1.5 mg%, bilirubin less than 1.0 mg, and SGOT less than 50 IU, are required. (Protocol closed to patients with squamous cell carcinoma of the cervix in April 1978 and to those with epithelial ovarian carcinoma in August 1978.)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dianhydrogalactitol, DAG, NSC-132313.

STRATIFICATION BY: Participating institutions, disease site.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 25 evaluable patients per disease site will be entered.

DOSAGE SCHEDULE:

DAG - 60 mg/sqm iv push q 7 days. If no toxicity occurs after 4 doses, increase to 75 mg/sqm/week. Continue therapy until evidence of disease progression or adverse effects.

DOSAGE FORMS: DAG - 50 mg vials.

DATE SUMMARIZED: 04/78

PATIENT ACCRUAL: 00960179

4.0073 PHASE II CHEMOTHERAPY WITH BAKER'S ANTIFOL FOR ADVANCED RECURRENT PELVIC MALIGNANCIES

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) GOG-26F

OBJECTIVES:

I. Determine efficacy of Baker's antifol for advanced pelvic malignancies resistant to current high priority methods of treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, recurrent, persistent, local or metastatic gynecologic cancer with documented disease progression who are not eligible for a higher priority protocols. Patients must have: GOG performance status no higher than 3; recovered from effects of recent surgery, radiotherapy, or chemotherapy (off chemotherapy for at least 3 weeks); adequate bone marrow function, and normal liver function (bilirubin less than 1.2 mg%). (Protocol closed to patients with squamous cell carcinoma of the cervix in February 1979 and to those with epithelial ovarian carcinoma in January 1980.)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Baker's Antifol, TZT, NSC-139105.

STRATIFICATION BY: Participating institution; disease site.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, response/remission rate, length of survival, toxicity/morbidity of treatment, progression-free interval.

CURRENT STATUS: 25 evaluable patients per disease site will be accrued.

DOSAGE SCHEDULE:

TZT - 500 mg/sqm iv infusion over 30-60 minutes once a week for 3 weeks as permitted by toxicity. Patients remain on study until disease progression or adverse effects prohibit further therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TZT - 100 and 250 mg vials.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00390179

4.0074 PHASE II CHEMOTHERAPY WITH ICRF-159 FOR ADVANCED RECURRENT PELVIC MALIGNANCIES

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PROTOCOL NUMBER(S) GOG-26G

OBJECTIVES:

I. Determine the efficacy of ICRF-159 for advanced pelvic malignancies resistant to current high priority methods of treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, recurrent, persistent local or metastatic gynecologic cancer with documented disease progression who are not eligible for a higher priority protocols. Patients must have: GOG performance status no higher than 3; recovered from effects of recent surgery, radiotherapy, or chemotherapy (off chemotherapy for at least 3 weeks); adequate bone marrow function, and normal liver function (bilirubin less than 1.2 mg%). (Protocol closed to patients with squamous cell carcinoma of the cervix in November 1979 and to those with epithelial ovarian carcinoma in June 1980.)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. ICRF-159, NSC-129943.

STRATIFICATION BY: Participating institution; disease site.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, response/remission rate, length of survival, toxicity/morbidity of treatment, progression-free interval.

CURRENT STATUS: 25 evaluable patients per disease site will be accrued.

DOSAGE SCHEDULE:

ICRF-159 - 2.5 g/sqm/day divided into 3 doses given q 6 hours on day 1 q week for 4 weeks as bone marrow recovery permits. Patients remain on study until disease progression or adverse effects prohibit further therapy. (Starting dose modified to 1.5 g/sqm, if toxicity not above grade 1 escalate to 2.0 g/sqm in course 2, to a maximum dose of 2.5 g/sqm in course 3. Addendum, November 1978)

Dosage modifications for toxicity are given.

DOSAGE FORMS: ICRF-159 - 50 and 500 mg scored tablets.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00380179

4.0075 PHASE II CHEMOTHERAPY WITH MAYTANSINE FOR ADVANCED RECURRENT PELVIC MALIGNANCIES

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Market Street, Suite 430, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) GOG-26H

OBJECTIVES:

I. Determine the efficacy of maytansine for advanced pelvic malignancies resistant to current high priority methods of treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, recurrent, persistent local or metastatic gynecologic cancer with documented disease progression who are not eligible for a higher priority protocol. Patients must have: a GOG performance status no higher than 3; recovered from effects of recent surgery, radiotherapy or chemotherapy (off chemotherapy for at least 3 weeks); adequate bone marrow function, and normal liver function (bilirubin less than 1.2 mg%). (Protocol closed to patients with squamous cell carcinoma of the cervix in August 1979.)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Maytansine, MTS, NSC-153858.

STRATIFICATION BY: Participating institution; disease site.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Objective tumor response, response/remission rate, length of survival, toxicity/morbidity of treatment, progression-free interval.

CURRENT STATUS: 25 evaluable patients per disease site will be accrued.

DOSAGE SCHEDULE:

MTX - 1.2 mg/sqm iv on day 1. Repeat course q 3 weeks and escalate dosage to a maximum of 2.0 mg/sqm as toxicity permits. Patients remain on study until disease progression or adverse effects prohibit further therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTS - 0.25 mg vials.

DATE SUMMARIZED: 12/78

PATIENT ACCRUAL: 00250179

4.0076 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED, RECURRENT PELVIC MALIGNANCIES

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Market Street, Suite 430, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) GOG-26I

OBJECTIVES:

I. Determine the efficacy of AMSA for advanced pelvic malignancies resistant to current high-priority methods of treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, recurrent, persistent local or metastatic gynecologic cancer with documented disease progression who are not eligible for a higher priority protocol. Patients must have: GOG performance status no higher than 3; recovered from effects of recent surgery, radiotherapy, or chemotherapy (off chemotherapy for at least 3 weeks); adequate bone marrow and renal function, and normal liver function (bilirubin less than 1.2 mg%).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, response/remission rate, length of survival, toxicity/morbidity of treatment, progression-free interval.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm (90 mg/sqm for patients with prior pelvic and/or abdominal radiotherapy) iv q 4 weeks as toxicity permits, if wbc at least 4000, platelets at least 100,000. Allow up to 8 weeks for recovery from toxicity. Consider one 4-week course an adequate trial. Continue therapy until disease progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg vials.

DATE SUMMARIZED: 06/79

4.0077 PHASE II CHEMOTHERAPY WITH YOSHI-864 FOR ADVANCED, RECURRENT PELVIC MALIGNANCIES

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Market Street, Suite 430, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) GOG-26J

OBJECTIVES:

I. Determine the efficacy of Yoshi-864 for advanced pelvic malignancies resistant to current high-priority methods of treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, recurrent, persistent local or metastatic gynecologic cancer with documented disease progression who are not eligible for a higher priority protocol. Patients must have: GOG performance status no higher than 3; recovered from effects of recent surgery, radiotherapy, or chemotherapy (off chemotherapy for at least 3 weeks); adequate bone marrow and renal function, and normal liver function (bilirubin less than 1.2 mg%).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Yoshi-864, YOSHI, NSC-102627.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, response/remission rate, length of survival, toxicity/morbidity of treatment, progression-free interval.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

YOSHI - 2 mg/kg/day iv on days 1 through 5 q 6 weeks as toxicity permits or until disease progression. Consider one 6-week course an adequate trial.

Dosage modifications for toxicity are given.

DOSAGE FORMS: YOSHI - 100 mg vials.

DATE SUMMARIZED: 06/79

4.0078 PHASE II CHEMOTHERAPY WITH CHLOROZOTOCIN FOR ADVANCED, RECURRENT AND METASTATIC PELVIC MALIGNANCIES IN PROGRESSION

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Market Street, Suite 430, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) GOG-26K

OBJECTIVES:

I. Determine the effects of chlorozotocin on advanced recurrent persistent metastatic or local gynecologic cancer in progression which is resistant to higher priority treatments.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, advanced as well as recurrent persistent, metastatic or local gynecologic cancer with documented disease progression who are not eligible for higher priority therapy. All primary gynocologic disease sites are eligible. Patients must have a Karnofsky performance status of at least 30, adequate bone marrow and kidney function, and normal liver function. Patients must not have had prior treatment with the protocol drug. They must have recovered from the effects of any prior therapy or surgery and must have concluded any prior chemotherapy 3 weeks ago.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

STRATIFICATION: None.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

CLZ - 100 mg/sqm (120 mg/sqm for patients who have received no prior chemotherapy) iv bolus q 6 weeks. Keep patients on study until disease progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLZ - 50 mg vials.

DATE SUMMARIZED: 11/79

4.0079 SURGICAL AND PATHOLOGICAL STUDY OF STAGES I-IV RESECTABLE SQUAMOUS CELL CARCINOMA OF THE VULVA

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PROTOCOL NUMBER(S) GOG-7711; GOG-36

OBJECTIVES:

I. Determine by observations of 5-year survival and disease free interval the validity of current FIGO staging, the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor in millimeters, histologic grade, and site and number of positive lymph nodes in Stage I through IV invasive squamous cell carcinoma of the vulva.

II. Accumulate rapidly prospectively significant surgical pathologic data to expedite development of further protocols for subsets of disease identified.

III. Determine the morbidity of primary radical surgical therapy.

PROTOCOL ENTRY CRITERIA: Patients with primary, previously untreated, totally resectable, histologically confirmed, invasive squamous cell carcinoma of the vulva clinically determine to be Stages I through IV.

PROTOCOL OUTLINE: Nonrandomized study.

Surgery. Radical vulvectomy and bilateral groin dissection.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Carcinoembryonic antigens, lymphangiogram, IVP, sigmoidoscopy, or cytoscopy.

END POINTS: Disease-free interval, time to recurrent, survival time, performance status, morbidity of treatment.

CURRENT STATUS: 200 patients will be entered per year.

DOSAGE SCHEDULE: Radical vulvectomy and bilateral groin dissection. Follow up patients with negative groin nodes q 3 months for 3 years and q 6 months for the next 2 years. Enter patients with positive groin nodes to protocol GOG-7712.

Dosage modifications for toxicity are not applicable.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 00810179

4.0080 RADIATION THERAPY VS PELVIC NODE RESECTION FOR INVASIVE SQUAMOUS CELL CARCINOMA OF THE VULVA WITH POSITIVE GROIN NODES

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PROTOCOL NUMBER(S) GOG-7712; GOG-37

OBJECTIVES:

I. Compare the efficacy of pelvic node resection vs. bilateral groin and pelvic node irradiation for invasive squamous-cell carcinoma of the vulva in patients having positive groin nodes.

PROTOCOL ENTRY CRITERIA: Nonpregnant women with primary, previously untreated, histologically confirmed squamous-cell carcinoma of the vulva who have undergone radical vulvectomy plus bilateral groin dissection to remove all of the local lesion with nodal metastases in one or both sides of the groin discovered at surgery. Patients entered on Protocol GOG-7711 who have positive groin nodes are eligible. Patients must not have recurrent or metastatic disease, been treated previously with pelvic irradiation, have a wbc of less than 4000, or platelets less than 150,000, or signs of renal impairment.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery. Deep pelvic node dissection on sides containing positive nodes only.

Arm II: Radiotherapy. Megavoltage (1 MeV or greater) to bilateral groin and pelvic nodes.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Renal function tests, liver function tests, CEA. Optional parameters include lymphangiogram, IVP, sigmoidoscopy, cystoscopy.

END POINTS: Recurrence rate, survival rate, subjective status on GOG Performance Scale, time to recurrence, survival time, morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Use surgical technique as outlined by Parsons and Ulfelder.

Arm II: Begin within 12 weeks of surgery. Radiotherapy - 4500-5000 rads given in 4.5 to 6 weeks to midplane of pelvis halfway between the superior border of the obturator foramena and Ls-S1 interspace. Electron beams may be used for anterior boosts of 4500 to 5000 rads tumor dose given in 4.5 to 6 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00100179

4.0081 PHASE II CHEMOTHERAPY WITH PAC (CIS-PLATINUM/ADRIAMYCIN/CYCLOPHOSPHAMIDE) FOR OVARIAN OR ENDOMETRIAL CARCINOMA

Carter, S. K., (415-497-7512) Northern California Oncology Group, 1801 Page Mill Rd., Bldg. B Suite 200, Palo Alto, California, 94304, United States of America

PROTOCOL NUMBER(S) NCOG-5O81

OBJECTIVES:

I. Determine the effectiveness of a combination of PAC: cis-platinum (CACP)/adriamycin (ADR)/cyclophosphamide (CTX) in patients with ovarian carcinoma or endometrial carcinoma in regard to response rate and duration response.

II. Assess the toxicity of PAC and gain experience with its use preliminary to employing it as first line therapy in future randomized trials.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically documented Stage III or IV ovarian carcinoma or endometrial carcinoma no longer amenable to surgery or radiotherapy, or with recurrent disease following alkylating or progestational agents. Patients must not have had radiation or chemotherapy within the preceding 4 weeks. Patients must have adequate bone marrow, renal, and cardiac status and a Karnofsky performance status equal to or greater than 50 percent.

PROTOCOL OUTLINE: Nonrandomized study.

Induction and Maintenance: 3-Drug Combination Chemotherapy. PAC: cis-Platinum, CACP, NSC-119875; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Audiometry, IVP, lymphangiogram, CAT scan, abdominal/pelvic ultrasound, LDH.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response, duration of response, survival time.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE: PAC: CACP - 60 mg/sqm iv 24-hour infusion with hydration and furosemide on day 1; ADR - 50 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on day 1; CTX - 600 mg/sqm iv on day 1. Repeat course q 28 days. When maximum ADR dose is reached, continue therapy with CACP/CTX. Patients with disease progression after at least one course are off study. Patients in complete remission from ovarian carcinoma after 9 courses or 1 year may stop therapy if remission is verified surgically; additional therapy is given if residual tumor is present.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; ADR - 10 mg ampules; CTX - 100 and 500 mg ampules.

DATE SUMMARIZED: 04/80

4.0082 PHASE II CHEMOTHERAPY WITH AMSA FOR METASTATIC OR RECURRENT EPITHELIAL CARCINOMA OF THE OVARY, ENDOMETRIUM, CERVIX, VAGINA, AND VULVA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7958

OBJECTIVES:

I. Determine the activity of AMSA for metastatic or recurrent epithelial carcinomas of the ovary, endometrium, cervix, vagina, or vulva that have failed to respond to higher priority protocols.

II. Determine the nature and degree of toxicity of AMSA in patients treated by the split-course 3-day schedule.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven, incurable, advanced metastatic or recurrent epithelial carcinoma of the ovary, endometrium, cervix, vagina or vulva. Patients must have a minimum life expectancy of 6 weeks, with a SWOG performance status of 2 or better and adequate hematologic, renal and hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions, prior adriamycin therapy.

SPECIAL STUDY PARAMETERS: IVP, hepatic and renal function, pelvic or abdominal scan.

END POINTS: Objective tumor response, response/remission rate, duration of response, relapse rate, duration of survival.

CURRENT STATUS: At least 42 patients to be entered.

DOSAGE SCHEDULE:

AMSA - 40 mg/sqm (poor risk patients, those over 65 years old, impaired bone marrow reserve, prior pelvic irradiation, poor hepatic or renal function start at 30 mg/sqm) iv on days 1 through 3. Repeat course q 21 days or as toxicity permits. Remove from study patients with progressive disease or unacceptable toxicity. Follow all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 02/80

4.0083 PHASE II EVALUATION OF AMSA IN PATIENTS WITH ADVANCED GYNECOLOGIC MALIGNANCIES

Brenner, D. E., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7910

OBJECTIVES:

I. Determine the therapeutic efficacy of m-AMSA in the treatment of patients with advanced gynecologic malignancies.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven, previously treated ovarian epithelial carcinomas or advanced cervical or endometrial carcinomas refractory to established therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-6, SMA-12, creatinine, clotting studies, EKG, chest x-ray, liver-spleen scan, bone scan, CT scan of head, bone marrow biopsy/aspiration as indicated, total abdominal CT scan, IVP, culdocentesis or peritoneal washings for cytology.

END POINTS: Response/remission rate, objective tumor response, duration of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv over 60 minutes. Repeat q 21 days.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

4.0084 ADJUNCT IMMUNOTHERAPY WITH VIRAL ONCOLYSATE FOR CARCINOMA OF THE CERVIX AND VULVA

Friedman, R. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-218

OBJECTIVES:

I. Evaluate viral modified tumor cell membrane extract (viral oncolysate) in two clinical conditions: In patients with vulvar carcinoma following radical vulvectomy and lymph-adenectomy with two or more positive lymph nodes, and in patients with squamous carcinoma of the uterine cervix (Stages IIB and IIIB) as an adjuvant to radiation therapy in a randomized study.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed lesions of primary vulvar carcinoma who have undergone radical vulvectomy and lymphadenectomy yielding 2 or more positive nodes (Group A), or with squamous cell carcinoma of the uterine cervix, Stages IIB or IIIB, who have undergone radiotherapy (Group B).

PROTOCOL OUTLINE: Randomized study, for Group B patients only. Enter Group A patients to Regimen A; randomize Group B patients to Arm I or II.

Regimen A: Immunotherapy. Viral modified tumor cell membrane extract (viral oncolysate), VMTCE.

Arm I: Radiotherapy plus Immunotherapy. VMTCE.

Arm II: Radiotherapy.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: In vitro humoral and cell-mediated studies, hypersensitivity tests with nonviable extracts of allogeneic tumor cells.

END POINTS: Disease-free interval, metastatic rate, survival time.

CURRENT STATUS: About 90 patients will be entered in over 2 years.

DOSAGE SCHEDULE:

Regimen A: VMTCE - dosage not given, id q 14 days for 2 years. Compare results with historical controls.

Arm I: VMTCE - dosage not given, id q 7 days for 12 months, plus Radiotherapy (details not given).

Arm II: Radiotherapy (details not given).

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/79

4.0085 PHASE II CHEMOTHERAPY WITH YOSHI-864 FOR CARCINOMA OF THE CERVIX, ENDOMETRIUM, OR OVARY

Wharton, J. T., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-304; MDA-G-7805

OBJECTIVES:

I. Determine the activity of Yoshi-864 in selected patients with carcinoma of the cervix, endometrium, or ovary.

II. Further investigate the toxicity of this drug following irradiation therapy, chemotherapy, abdominal surgery or a combination of these treatments.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven measurable carcinoma of the cervix or endometrium who are not eligible for radiotherapy or surgery and who have failed prior chemotherapy, or patients with adenocarcinoma of the ovary Stages III or IV who have failed to respond to 1st and 2nd line chemotherapy programs. Patients must have adequate hematologic, liver, and kidney function. All prior therapy must have terminated at least 4 weeks prior to study entry and patients must have recovered from the toxic effects.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Yoshi-864, YOSHI, NSC-102627.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response.

CURRENT STATUS: 52 patients will be entered in 9 months.

DOSAGE SCHEDULE:

YOSHI - 70 mg/sqm/day iv on days 1 through 5 q 6 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/79

SECTION 5

MYELOMA AND OTHER HEMATOLOGIC TUMORS

5A. MYELOMA

CLB-7761 SEQUENTIAL VS CONCURRENT L-PAM/CTX/BCNU/PRED CHEMOTHERAPY WITH AND WITHOUT ADR VS L-PAM ALONE FOR MULTIPLE MYELOMA 5.0001

CLB-8003 PILOT CHEMOTHERAPY WITH MELPHALAN/PREDNISONE PLUS TOTAL BONE MARROW IRRADIATION FOR MULTIPLE MYELOMA 5.0002

CLB-8074 PHASE II CHEMOTHERAPY WITH AMSA FOR MULTIPLE MYELOMA RESISTANT TO MELPHALAN AND PREDNISONE 5.0003

EST-2479 PHASE III CHEMOTHERAPY WITH MP (L-PAM/PRED) VS VBMCP (VCR/BCNU/L-PAM/CTX/PRED) FOR UNTREATED MULTIPLE MYELOMA 5.0004

EST-3477 PHASE II MASTER PROTOCOL AND CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE OR HEXAMETHYLMELAMINE FOR MULTIPLE MYELOMA 5.0005

SEG-MM-P37 PHASE I-II HEMI-BODY RADIOTHERAPY PLUS PREDNISONE FOR MULTIPLE MYELOMA REFRACTIVE OR RESISTANT TO CHEMOTHERAPY 5.0006

SEG-76MM0203 PHASE III CHEMOTHERAPY WITH BCNU/CTX/PRED FOLLOWED BY ADR/VCR/AZA/PRED VS NO THERAPY VS L-PAM/PRED FOR PREVIOUSLY UNTREATED MULTIPLE MYELOMA 5.0007

SEG-80MM265 PHASE II STUDY OF CLZ AND PRED IN THE TREATMENT OF REFRACTORY MULTIPLE MYELOMA 5.0008

SWOG-7719 PHASE II TRIAL OF ADDITION OF CACP AND BLEO TO VBAP (VCR/BCNU/ADR/PRED) AND MAINTENANCE WITH L-PAM/PRED FOR RELAPSING AND RESISTANT MYELOMA 5.0009

SWOG-7927/28 PHASE III CHEMOTHERAPY WITH VARIOUS COMBINATIONS OF VCR, L-PAM, CTX, BCNU, ADR, PRED, AND LEV FOR MULTIPLE MYELOMA 5.0010

BCRP-8001 INDUCTION CHEMOTHERAPY WITH ADR/BCNU/CTX/VBL/PRED AND HIGH-DOSE CTX/VCR/PRED PLATEAU-PHASE MAINTENANCE FOR MULTIPLE MYELOMA 5.0011

MDAR-274 CHEMOTHERAPY WITH INVESTIGATIONAL DRUGS AND L-PAM/PRED FOR UNRESPONSIVE MULTIPLE MYELOMA 5.0012

MDAR-423 PHASE II EVALUATION OF VINDESINE IN THE TREATMENT OF REFRACTORY MULTIPLE MYELOMA IN ADULTS 5.0013

MSKCC-7218B COMBINATION CHEMOTHERAPY WITH BCNU/CTX/L-PAM/VCR PLUS PREDNISONE FOR PROGRESSIVE GENERALIZED MYELOMA 5.0014

NCI-80-C-69 PHASE I-II STUDY OF TOTAL BODY IRRADIATION FOR MULTIPLE MYELOMA RESISTANT TO SYSTEMIC CHEMOTHERAPY 5.0015

NY-ACSCS-1 IMMUNOTHERAPY WITH INTERFERON FOR MULTIPLE MYELOMA 5.0016

CAN-NCIC-MY2 COMBINATION CHEMOTHERAPY WITH L-PAM/PRED AND CTX/PRED OR CCNU/VCR/PRED/ADR MAINTENANCE FOR MULTIPLE MYELOMA 5.0017

5B. HISTIOCYTOSIS

CCG-984 PHASE III INDUCTION AND MAINTENANCE CHEMOTHERAPY WITH PRED/VBL/MTX/CTX AND MTX/CTX/6-MP FOR HISTIOCYTOSIS X IN CHILDREN 5.0018

5C. POLYCYTHEMIA VERA

PVSG-8 PHASE II CHEMOTHERAPY WITH HYDROXYUREA FOR POLYCYTHEMIA VERA .. 5.0019

5D. MYCOSIS FUNGOIDES

SWOG-7622R PHASE II CHEMOTHERAPY WITH CTX/ADR/VCR/PRED/BLEO FOLLOWING RADIOTHERAPY FOR STAGE I MYCOSIS FUNGOIDES 5.0020

5E. OTHER HEMATOLOGIC MALIGNANCIES

PVSG-12 PHASE II CHEMOTHERAPY WITH HYDROXYUREA FOR POLYCYTHEMIA VERA, MYELOFIBROSIS AND PRIMARY THROMBOCYTOSIS 5.0021

MSKCC-7827 PHASE II STUDY OF CIS-PLATINUM FOR NON-HODGKIN'S HEMATOLOGIC MALIGNANCIES 5.0022

SECTION 5

MYELOMA AND OTHER HEMATOLOGIC TUMORS

5A. MYELOMA

5.0001 SEQUENTIAL VS CONCURRENT L-PAM/CTX/BCNU/PRED CHEMOTHERAPY WITH AND WITHOUT ADR VS L-PAM ALONE FOR MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) CLB-7761

OBJECTIVES:

I. Test the hypothesis that three alkylating agents given sequentially produce higher frequency of good response and longer duration of disease control than the same alkylating agents given in combination in patients with multiple myeloma.

II. Test the hypothesis that addition of adriamycin to a combination of three alkylating agents increases the frequency of good response and prolongs the duration of disease control.

III. Test the hypothesis that the frequency of good response and the duration of disease control are the same after treatment with intravenous L-PAM as after treatment with triple alkylating agents.

IV. Compare the duration of remission maintained with oral L-PAM in patients induced with combination chemotherapy regimens and with intravenous L-PAM and compare duration of disease control with these regimens against historical controls maintained on intravenous therapy with triple alkylating agents.

V. Evaluate psychosocial function in patients with myeloma before and during treatment and investigate differences in psychosocial function in patients receiving different treatment.

VI. Determine whether new experimental regimens prolong the survival of patients with multiple myeloma compared to historical controls.

PROTOCOL ENTRY CRITERIA: Patients with morphologically and clinically proven multiple myeloma, who have had no prior therapy with study agents.

PROTOCOL OUTLINE: Randomized study. Randomize all patients to Induction therapies I, II, III, or IV, then enter all patients to Maintenance, Arm V.

Induction: (Patient entry suspended temporarily, Addendum 2, June 1978; study resumed, Addendum 3, July 1978).

Arm I: Concurrent 3-Drug Combination Chemotherapy plus Hormone Therapy. Melphalan, L-PAM, NSC-8806; Cyclophosphamide, CTX, NSC-26271; BCNU, NSC-409962; plus Prednisone, PRED, NSC-10023.

Arm II: Sequential 3-Drug Combination Chemotherapy, plus Hormone Therapy. L-PAM; CTX; BCNU; plus PRED.

Arm III: 4-Drug Combination Chemotherapy plus Hormone Therapy. L-PAM; CTX; BCNU; Adriamycin, ADR, NSC-123127; plus PRED.

Arm IV: Single-agent Chemotherapy plus Hormone Therapy. L-PAM; plus PRED.

Maintenance:

Arm V: Single-agent Chemotherapy. L-PAM.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: M serum and urinary proteins, marrow plasma cells, skeletal survey, EKG.

END POINTS: Response/remission rate, duration of response, survival time, survival rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: About 440 patients will be entered in about 28 months.

DOSAGE SCHEDULE:

Arm I: L-PAM - 8 mg/sqm iv on day 1; CTX - 300 mg/sqm iv on day 1; BCNU - 100 mg/sqm iv on day 1; PRED - 0.8 mg/kg po on days 1 through 14, 0.4 mg/kg po on days 15 through 28, 0.2 mg/kg po on days 29 through 42, then discontinue. Repeat course with L-PAM, CTX and BCNU q 6 weeks for a total of 12 courses.

Arm II: L-PAM - 16 mg/sqm iv on day 1; CTX - 600 mg/sqm iv on day 22; BCNU - 150 mg/sqm iv on day 43. PRED - 6-week course as in Arm I. Repeat course with L-PAM, CTX and BCNU for a total of 6 courses.

Arm III: L-PAM, CTX and BCNU, dosage as in Arm I, give only on days 1, 43, 106, 148, 211, 253, 316, 358, 421 and 463. ADR - 45 mg/sqm iv given on days 85, 290, 295 and 400. PRED, as in Arm I.

Arm IV: L-PAM - 16 mg/sqm iv on days 1, 15, 29, 43, 71 and q 4 weeks thereafter until day 491 for a total of 20 doses. PRED - as in Arm I.

Enter all patients exiting from Arms I, II, III and IV to Arm V in week 73.

Arm V: L-PAM - 0.05 mg/kg/day po until documented relapse or disease progression or until 2 years from the first day of induction by chemotherapy.

Patients with unacceptable toxicity or those needing radiation therapy to more than one involved area are removed from study.

Dosage modifications for toxicity are given (see Addendum 1, October 28, 1978).

DOSAGE FORMS: L-PAM - 50 mg vials and 2 mg tablets; ADR - 10 and 50 mg vials; CTX - 100, 200 and 500 ml vials; BCNU - 100 mg vials; PRED - 5, 10 and 20 mg tablets.

DATE SUMMARIZED: 04/79

PATIENT ACCRUAL: 01601078

5.0002 PILOT CHEMOTHERAPY WITH MELPHALAN/PREDNISONE PLUS TOTAL BONE MARROW IRRADIATION FOR MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) CLB-8003

OBJECTIVES:

I. Determine the response to treatment consisting of a program of oral melphalan/prednisone chemotherapy followed by total bone marrow irradiation in patients with multiple myeloma.

II. Monitor the toxic side effects of this form of treatment and determine the practicality of administering total bone marrow irradiation.

PROTOCOL ENTRY CRITERIA: Patients with an unequivocal diagnosis of multiple myeloma who have not received prior radiation therapy, alkylating agents or nitrosoureas. Patients may have received prior corticosteroid therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Hormone Therapy plus Radiotherapy. Melphalan, L-PAM, NSC-8806; plus Prednisone, PRED, NSC-10023; plus total bone marrow irradiation with megavoltage, 4 MeV or greater photons and electrons.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Bone marrow aspiration and biopsy, total serum protein and electrophoresis, skeletal survey.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response, recurrence rate, duration of response, length of survival.

CURRENT STATUS: 16 patients will be entered.

DOSAGE SCHEDULE:

L-PAM - 150 mcg/kg/day po on days 1 through 7, 50 mcg/kg/day po weeks 4 through 12; PRED - 0.8 mg/kg/day po weeks 1 and 2, 0.4 mg/kg/day po weeks 3 and 4, 0.2 mg/kg/day po weeks 5 and 6. Following a 4-week rest period, give photon beam radiation - a total of 750 rads (150 rads per session for 5 consecutive sessions) to each of 3 body segments. Rest for 4 weeks, then 750 rads similarly to each of 2 body segments. Rest for 4 weeks. Electron beam radiation - a total of 1500 rads (150 rads in 10 consecutive sessions) to both cranium and ribs (that volume not included in the photon field). All patients will be followed until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-PAM - 2 mg tablets; PRED - 5, 10 and 20 mg tablets.

DATE SUMMARIZED: 12/80

5.0003 PHASE II CHEMOTHERAPY WITH AMSA FOR MULTIPLE MYELOMA RESISTANT TO MELPHALAN AND PREDNISONE

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PROTOCOL NUMBER(S) CLB-8074

OBJECTIVES:

I. Determine the response rate of multiple myeloma resistant to melphalan and prednisone or other alkylating agents to treatment with m-AMSA as judged by the frequency of partial or complete objective response.

II. Determine the duration of response in those patients continuing on m-AMSA.

III. Provide additional clinical and laboratory data regarding toxicity.

PROTOCOL ENTRY CRITERIA: Patients with unequivocal multiple myeloma who have been previously treated with melphalan, adriamycin, cyclophosphamide, nitrosourea and prednisone and have failed to respond or have relapsed. Patients must have adequate hematologic and hepatic function (bilirubin greater than 3.2 mg/dl) and life expectancy of 2 months. Patients must not have any other diseases characterized by plasmacytosis of bone marrow or be receiving corticosteroids in amounts greater than 20 mg/day unless for hypercalcemia. Patients must not have had radiotherapy for 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions (participation open to all Group institutions).

SPECIAL STUDY PARAMETERS: Tumor measurement; bone marrow biopsy and aspirate; serum and urinary protein electrophoresis; metastatic roentgenographic survey; hematologic, hepatic, and renal function tests.

END POINTS: Objective response/remission rate (Myeloma Task Criteria), duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 25-30 qualified cases will be entered.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv in a 60-minute infusion q 3 weeks. Patients with bone marrow depression and abnormal hepatic function receive initial doses reduced up to 75 percent and 50 percent, respectively. Those showing response or stable disease continue treatment until relapse or progression; those with progressive disease after 3 courses at the maximum tolerated dose are off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 20 and 50 mg vials.

DATE SUMMARIZED: 08/80

5.0004 PHASE III CHEMOTHERAPY WITH MP (L-PAM/PRED) VS VBMCP (VCR/BCNU/L-PAM/CTX/PRED) FOR UNTREATED MULTIPLE MYELOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-2479

OBJECTIVES:

I. Compare effects of melphalan (L-PAM)/prednisone (PRED) vs. vincristine (VCR)/BCNU/L-PAM/cyclophosphamide (CTX)/-PRED for previously untreated multiple myeloma.

PROTOCOL ENTRY CRITERIA: Patients with multiple myeloma confirmed by the presence of bone marrow plasmacytosis with at least 10% plasma cells or biopsy-proven plasmacytoma plus at least one of following: myeloma protein in serum, myeloma protein in urine, or radiologic evidence of osteolytic lesions. Disease must be measurable by serum M-component greater than 1.0 gm/100 ml, urine monoclonal light chain excretion greater than 200 mg/24 hrs, or serially measurable soft tissue plasmacytoma. Patients must have adequate liver function and must not have had prior chemotherapy except for PRED or Mithramycin for hypercalcemia.

PROTOCOL OUTLINE: Randomized study for Induction only.

Induction:

Arm I: Single-agent Chemotherapy plus Hormone Therapy. Melphalan, L-PAM, NSC-8806; plus Prednisone, PRED, NSC-10023.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; BCNU, NSC-409962; L-PAM; Cyclophosphamide, CTX, NSC-26271; plus PRED.

STRATIFICATION: Participating institutions; age: under 65 years vs. 65 and over; renal function: creatinine less than 2.0 vs. 2.0 and over; clinical stage: I vs. II vs. III.

SPECIAL STUDY PARAMETERS: Pain grade, bone marrow, aspirate and biopsy, serum protein electrophoresis, serum quantitative immunoglobulins, serum and urine M-protein immunoelectrophoresis, urine light chain excretion.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: At least 116 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Induction:

Arm I: L-PAM - 8 mg/sqm po on days 1 through 4; PRED - 60 mg/sqm po on days 1 through 4; both given q 28 days for 13 courses. Crossover to Arm II Induction patients who show progression after 2 courses and to Arm II Maintenance patients who show no response after 13 courses.

Arm II: VCR - 1.2/mg/sqm (maximum single dose 2.0 mg) iv on day 1; BCNU - 20 mg/sqm iv on day 1; L-PAM - 8 mg/sqm po on day 1 through 4; CTX - 400 mg/sqm iv on day 1; PRED - 40 mg/sqm po on days 1 through 7 plus 20 mg/sqm po on days 8 through 14 of the first 3 courses; all given q 35 days for 10 courses. Remove from study patients in progression after 2 courses or who show no response after 10 courses.

Maintenance: Enter patients with continued objective response after 12 months of Induction. Follow until relapse but give no therapy to patients who were Stage I at time of initial randomization and who have no residual M-protein in serum or urine. Repeat respective induction courses at less frequent intervals for patients who were Stage II or III at time of initial randomization or patients who were Stage I but have residual M-protein in serum or urine: 1 course q 6 weeks for 3 courses, then 1 course q 8 weeks until relapse.

Remove from study patients with intolerable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-PAM - 1 mg tablets; CTX - 100, 200 and 500 mg vials; BCNU - 100 mg vials; VCR - 1 and 5 mg ampules; PRED - 5, 20 and 50 mg tablets.

DATE SUMMARIZED: 11/79

5.0005 PHASE II MASTER PROTOCOL AND CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE OR HEXAMETHYLMELAMINE FOR MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) EST-3477

OBJECTIVES:

I. Establish a master protocol to evaluate anti-tumor activity of agents in patients with refractory multiple myeloma.

II. Evaluate chemotherapy with cyclophosphamide (CTX) for high risk patients (Regimen A) and hexamethylmelamine (HMM) for low risk patients (Regimen B) with multiple myeloma, using the treatment parameters of this master protocol.

PROTOCOL ENTRY CRITERIA: Patients with multiple myeloma as confirmed by medullary plasmocytosis and a monoclonal protein in the serum or urine. Patients must have evidence of a refractory response to previous standard chemotherapy, an estimated survival of at least 2 months, must not have received any chemotherapy within 4 weeks and no long-term corticosteroid therapy at any dose. In addition, patients to be entered to Regimen A (CTX) may be previously untreated, with at least 3 of 6 risk factors: BUN more than 30 mg percent and creatinine more than 2 mg percent, platelets less than 100,000/cumm, Hb less than 8.0 mg percent without G.I. bleeding, calcium ion more than 12.0 mg percent, performance status 3 or 4, or patients with plasma cell leukemia. Previously treated patients must have a wbc greater than 2000/cumm and a granulocyte count better than 1000/cumm. Patients should have stable kidney function. Patients entered to Regimen B (HMM) should have a wbc above 2000/cumm, platelets above 50,000/cumm, BUN less than 30, creatinine less than 20, bilirubin less than 1.5 and no active liver disease. (Regimen B closed to patient entry, Addendum 4, August 1980.)

PROTOCOL OUTLINE: Nonrandomized study. Assign high-risk patients with inadequate renal function, Hb, or platelet counts, a performance status of 3 or 4 or plasma cell leukemia greater than 10% to Regimen A. Assign low-risk patients to Regimen B. (Regimen B closed to patient entry, Addendum 4, August 1980.)

Regimen A: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271; plus Allopurinol, NSC-1390.

Regimen B: Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

STRATIFICATION BY: Participating institutions, BUN and creatinine levels, platelet counts, Hb and calcium levels, performance status, incidence of medullary plasmocytosis.

SPECIAL STUDY PARAMETERS: Measurement of plasma cells in bone marrow, renal function tests, serum protein electrophoresis, quantitative serum immunoglobulins, urinalysis for light chain proteins.

END POINTS: Response/remission rate, objective measurements of serum myeloma proteins, stability of disease, progression of disease.

CURRENT STATUS: 40-50 patients are to be entered.

DOSAGE SCHEDULE:

Regimen A: CTX - 600 mg/sqm iv on days 1 through 4, plus Allopurinol and hydration. Repeat cycle on day 29. Evaluate patients on day 57 and repeat cycle q 90 days for good responders for a total of 7 more cycles, or until complete response is obtained. Remove patients with disease progression at any time from study.

Regimen B: HMM - 200 mg/sqm po in 3 or 4 equally divided doses on days 1 through 21. Repeat cycle q 28 days and re-evaluate patients on day 57. Continue therapy for patients in remission until signs of relapse or unacceptable toxicity. (Regimen closed to patient entry, August 1980.)

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; HMM - 50 and 100 mg capsules.

DATE SUMMARIZED: 09/80

PATIENT ACCRUAL: 00150378

5.0006 PHASE I-II HEMI-BODY RADIOTHERAPY PLUS PREDNISONE FOR MULTIPLE MYELOMA REFRACTIVE OR RESISTANT TO CHEMOTHERAPY

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America

PROTOCOL NUMBER(S) SEG-MM-P37

OBJECTIVES:

I. Evaluate the toxicity and efficacy in the palliation of pain of hemi-body irradiation for uncontrolled multiple myeloma.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with a diagnosis of multiple myeloma based on bone marrow, serum and/or urine protein abnormalities, and/or bony lesions, who have measurable protein abnormality or tumor mass or moderate to severe pain. Patients must be unresponsive to current standard or Phase III regimens and they must have completed such therapy at least 4 weeks ago. Patients must have adequate bone marrow, kidney, and pulmonary and cardiac function, less than 20% deviation from normal liver function, and a Karnofsky performance status of at least 20%.

PROTOCOL OUTLINE: Nonrandomized study.

Hormone Therapy plus Radiotherapy. Prednisone, PRED, NSC-10023 plus irradiation of the upper and lower hemi-body with photons (1.2 MeV or higher beam energy).

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum protein electrophoresis, bone scan, pulmonary function, bone marrow aspirate and biopsy, urinary proteins, skeletal x-rays.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 29 to 44 patients will be entered in about 8 months.

DOSAGE SCHEDULE:

Pre-treat patients with 100 mg PRED on the day before and the day of Radiotherapy.

Phase I: Determine maximum tolerated dose (MTD) for each hemi-body by entering successive cohorts of 3 patients to 300 rads to one hemi-body with 100-rad increment escalation to a maximum of 7000 rads if no severe or life threatening complications occur. When peripheral counts return to pretreatment levels (approximately 6 weeks) determine MTD for other hemi-body in the same manner.

Phase II: To study pain relief treat other patients with one MTD for each hemi-body, as determined, maintaining time intervals between hemi-body irradiations as described above.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 10/79

5.0007 PHASE III CHEMOTHERAPY WITH BCNU/CTX/PRED FOLLOWED BY ADR/VCR/AZA/PRED VS NO THERAPY VS L-PAM/PRED FOR PREVIOUSLY UNTREATED MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) SEG-76MM0203; SEG-76MM311

OBJECTIVES:

I. Compare continuous therapy with intermittent therapy in myeloma after reducing initial plasma cell mass.

II. Determine the effect of a combination of non-alkylating agents, adriamycin, vincristine, and azathioprine (plus prednisone) in myeloma after plasma cell mass has been reduced by BCNU, cyclophosphamide and prednisone.

PROTOCOL ENTRY CRITERIA: Untreated patients with multiple myeloma with measurable serum and/or urine protein component with signs and/or symptoms of disease.

PROTOCOL OUTLINE: Randomized study for Maintenance only.

Induction: Enter all patients.

3-Drug Combination Chemotherapy: BCNU, NSC-409962; Cyclophosphamide, CTX, NSC-26271; Prednisone, PRED, NSC-10023.

Maintenance:

Arm I: 4-Drug Combination Chemotherapy: Adriamycin, ADR, NSC-123127; Azathioprine, AZA, NSC-39084; Vincristine, VCR, NSC-26271; Prednisone, PRED, NSC-10023.

Arm II: Control Group: No therapy.

Arm III: 2-Drug Combination Chemotherapy: Melphalan, L-PAM, NSC-8806; PRED.

STRATIFICATION BY: Good risk and poor risk.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction:

BCNU - 75 mg/sqm iv on day 1; CTX - 400 mg/sqm iv on day 1; PRED -75 mg po single dose on days 1 through 7. Repeat course q 4 weeks until plateau to find a stabilization of anomalous protein marker after 2 successive monthly determinations. Remove non-responders from study, randomize responders to Arms I, II, or III.

Maintenance:

Arm I: ADR - 30 mg/sqm iv on day 1; VCR - 1 mg/sqm iv on day 1 (maximum 2 mg); AZA - 100 mg/sqm po on days 1 through 7 (single dose, fasting); PRED - 75 mg/day po on days 1 through 5, single dose. Repeat course q 3 weeks for a total of 8 courses. Patients without disease progression will be followed 'off drugs'. If there is progression before 8 courses, remove patient from study, and treat with Reinduction therapy with BCNU/CTX/PRED.

Arm II: No therapy. Follow patients until disease progression and then treat with BCNU/CTX/PRED, as in Induction.

Arm III: L-PAM - 8 mg/sqm po on days 1 through 4 (single dose, fasting); PRED - 75 mg/day po on days 1 through 7 (single dose). If continuing to respond at the end of 6 monthly courses treatment is continued. If disease has progressed patient is reinduced with BCNU/CTX/PRED. If disease is stable at the end of 6 courses, therapy will be discontinued. Observe for relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; CTX - 100, 200, 500 mg vials; L-PAM - 2 mg tablets; ADR - 10, 50 mg vials; VCR - 1 mg ampules; AZA -50 mg tablets; PRED - 5, 20, 50 mg tablets.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00070077

5.0008 PHASE II STUDY OF CLZ AND PRED IN THE TREATMENT OF REFRACTORY MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) SEG-80MM265

OBJECTIVES:

I. Determine the response rate of patients with multiple myeloma to treatment with chlorozotocin plus prednisone.

II. Determine the toxicity of this regimen.

PROTOCOL ENTRY CRITERIA: Patients with multiple myeloma according to criteria of the SECSG Myeloma Committee. Patients must have been previously treated with and found to be unresponsive to current standard or Phase III SECSG study regimens for multiple myeloma. At least 6 weeks must have elapsed since previous BCNU treatment. Patients should have a measurable tumor mass and/or abnormal protein. Hematologic and renal function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Hormone Therapy. Chlorozotocin, CLZ, NSC-178248; Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Skeletal x-rays; measurement of plasmacytomas; hematologic parameters; bone marrow, liver and kidney tests; 24-hour urine and UEP; IEP for abnormal protein type; fasting blood sugar.

END POINTS: Response/remission rate, duration of response, toxicity of treatment, objective tumor response.

CURRENT STATUS: 195 patients will be required for the study.

DOSAGE SCHEDULE:

CLZ - 120 mg/sqm iv in rapidly flowing infusion on day 1; PRED - 75 mg/day po for 7 days. Repeat at 6-week intervals. If progression occurs after 2 courses (12 weeks), patient goes off study. If stability or improvement occurs after 2 courses, 2 more courses will be administered. If the patient has not achieved at least a fair improvement status after 4 courses, he will go off study; if a fair or excellent response occurs after 4 courses, treatment will be continued until disease progresses. An adequate trial of therapy will consist of 12 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLZ - 50 mg vials; PRED - 2, 20, and 50 mg tablets.

DATE SUMMARIZED: 06/80

5.0009 PHASE II TRIAL OF ADDITION OF CACP AND BLEO TO VBAP (VCR/BCNU/ADR/PRED) AND MAINTENANCE WITH L-PAM/PRED FOR RELAPSING AND RESISTANT MYELOMA

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PROTOCOL NUMBER(S) SWOG-7719; MDAR-264

OBJECTIVES: This protocol replaces protocols SWOG-7432 and MDAR-133.

I. Evaluate the efficacy of adding cis-platinum and bleomycin to VBAP (vincristine/BCNU/adriamycin/prednisone) in the treatment of patients with multiple myeloma who have failed to respond to or have relapsed on combinations of melphalan and/or cyclophosphamide with prednisone.

II. Compare the results with previous SWOG trials of VBAP in such patients.

PROTOCOL ENTRY CRITERIA: Patients with multiple myeloma who are no longer responding to or have not responded to melphalan and/or cyclophosphamide combined with prednisone. The minimum prior dose of melphalan is 3.2 mg/kg in 6 months, and that of cyclophosphamide is 6 g/sqm in 6 months. Patients must have evidence of progressive disease. There must be reasonable cardiac, renal, and pulmonary function. Patients must have recovered from prior radiation- or drug-induced myelotoxicity.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 5-Drug Combination Chemotherapy plus Hormone Therapy. VBAP: Vincristine, VCR, NSC-67574; BCNU, NSC-409962; Adriamycin, ADR, NSC-123127; Prednisone, PRED, NSC-10023; and Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

Maintenance: Single-agent Chemotherapy plus Hormone Therapy. Melphalan, L-PAM, NSC-8806; PRED.

STRATIFICATION BY: Participating institutions; response to prior melphalan/cyclophosphamide/prednisone therapy: no response vs. relapse.

SPECIAL STUDY PARAMETERS: Hemogram, bone marrow, kidney and liver function tests, total serum protein and M peak, urinary M peak, creatinine clearance, bone survey, chest x-ray, pulmonary function studies.

END POINTS: Response/remission rate, duration of response, objective tumor response, recurrence rate, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Eleven patients have been entered in 3 years.

DOSAGE SCHEDULE:

Induction: VBAP: VCR - 1 mg iv push on day 1; BCNU - 30 mg/sqm iv infusion over at least 15 minutes on day 1; ADR - 30 mg/sqm iv on day 1; PRED - 60 mg/sqm/day po on days 1 through 5; with BLEO - 7.5 mg im on days 2 through 5; and CACP - 20 mg/day iv infusion with mannitol diuresis on days 2 through 5. Repeat courses at 3-week intervals or after recovery of marrow. Minimum number of courses is 3, maximum 6. If patient continues to respond, continue treatment with VBAP plus CACP without BLEO until maximum reduction of myeloma protein has been reached.

Maintenance: Begin after maximum effect in Induction has been achieved. L-PAM - 6 mg/sqm/day for 4 days; PRED - 100 mg/day for 4 days. Repeat at 3-week intervals. At relapse, treat with VAP: VCR/ADR/PRED plus CACP.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 10 mg vials; BCNU - 10 mg vials; ADR - 10 and 50 mg vials; PRED - 5 and 50 mg tablets; CACP - 10 and 50 mg vials; BLEO - 15 unit vials.

DATE SUMMARIZED: 08/80

5.0010 PHASE III CHEMOTHERAPY WITH VARIOUS COMBINATIONS OF VCR, L-PAM, CTX, BCNU, ADR, PRED, AND LEV FOR MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) SWOG-7927/28; MDAR-377

OBJECTIVES:

I. Compare the effects of 4 drug combinations for remission induction in previously untreated patients with multiple myeloma: (1) VMCP: vincristine (VCR)/melphalan (L-PAM)/cyclophosphamide (CTX)/prednisone (PRED) followed by VBAP: VCR/BCNU/adriamycin (ADR)/PRED vs. (2) VMCP/levamisole (LEV) followed by VBAP/LEV vs. (3) VCP: VCR/CTX/PRED vs. (4) VCP/LEV.

II. Evaluate 12 months of Maintenance chemotherapy with VCP with and without LEV vs. similar, previous SWOG therapies.

PROTOCOL ENTRY CRITERIA: Patients previously untreated with chemotherapy with measurable disease and objective evidence and symptoms of complications of any stage of multiple myeloma. Enter asymptomatic patients only if they have a confirmed diagnosis and there is evidence of increasing tumor mass. Patients must have an adequate cardiac status.

PROTOCOL OUTLINE: Randomized study for Induction only. Randomize patients to Arms I, II, III and IV at the ratio of 1:2:2:2 respectively.

Induction:

Arm I: Sequential 3-Drug Combination Chemotherapy plus Hormone Therapy. VMCP: Vincristine, VCR, NSC-67574; Melphalan, L-PAM, NSC-8806; Cyclophosphamide, CTX, NSC-26271; plus Prednisone, PRED, NSC-10023; followed by VBAP: VCR; BCNU, NSC-409962; Adriamycin, ADR, NSC-123127; plus PRED.

Arm II: Sequential 3-Drug Combination Chemotherapy, Hormone Therapy plus Immunotherapy. VMCP; plus Levamisole, LEV, NSC-177023; followed by VBAP plus LEV.

Induction and Maintenance:

Arm III: 2-Drug Combination Chemotherapy plus Hormone Therapy. VCP: VCR; CTX; plus PRED.

Arm IV: 2-Drug Combination Chemotherapy plus Hormone Therapy plus Immunotherapy. VCP; plus LEV.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum and urine protein and electrophoresis, quantitative immunoglobulins, skeletal x-ray survey, M component typing by immunoelectrophoresis.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 266 patients will be entered in just over 18 months.

DOSAGE SCHEDULE:

Poor-risk patients (PRP) are those with prior large volume radiotherapy (e.g., hemipelvis, more than 5 thoracic and/or lumbar vertebrae) and/or over 70 years of age, and/or creatinine over 3.0.

Induction:

Arm I: VMCP: VCR - 1 mg iv on day 1; L-PAM - 5.5 mg/sqm (4 mg/sqm for PRP) po on days 1 through 4; CTX - 110 mg/sqm (80 mg/sqm for PRP) po on days 1 through 4. PRED - 60 mg/sqm po on days 1 through 4; all given q 21 days for 3 courses; followed by VBAP: VCR - 1 mg iv on day 1; BCNU - 30 mg/sqm (20 mg/sqm for PRP) iv on day 1; ADR - 30 mg/sqm (20 mg/sqm for PRP, maximum single dose 60 mg and cumulative dose 400 mg/sqm) iv on day 1; PRED - 60 mg/sqm po on days 1 through 4; all given q 21 days for 3 courses. Repeat VMCP/VBAP sequence for a minimum of 6 months and a maximum of 18 months.

Arm II: VMCP - as in Arm I; plus LEV - 50 mg 4 times/day po on days 8, 9, 15, and 16 repeated q 21 days for 3 courses; followed by VBAP - as in Arm I; plus LEV - as above, repeated q 21 days for 3 courses.

Arm III: VCP: VCR - 1 mg iv on day 1; CTX - 180 mg/sqm (120 mg/sqm for PRP) po on days 1 through 4; PRED - 60 mg/sqm po on days 1 through 4; all given q 21 days.

Arm IV: VCP - as in Arm III; LEV - as in Arm II.

Repeat courses in all arms for a minimum of 6 months and a maximum of 18 months. When patient achieves a 75% reduction of tumor size or myeloma protein production, enter patient to Maintenance. Remove from study patients without this response after 18 months.

Maintenance: Enter responders from Arms I and II to Arm III and responders from Arm II to Arm IV (responders on Arm IV continue on Arm IV), both q 21 days for 12 months. Discontinue Chemotherapy for patients in remission after 12 months of Maintenance only if there is a disappearance of the serum protein peak; otherwise continue Maintenance therapy indefinitely. Reinduce patients who relapse during unmaintained remission, using the same regimen to which they originally responded.

Remove from study patients who develop progressive disease after 2 or more courses of Induction; or who have less than 75% tumor reduction after 18 months of Induction; who relapse while on Maintenance; and who relapse on unmaintained remission and do not respond to reinduction. Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules; BCNU - 100 mg vials; CTX - 25 and 50 mg tablets; LEV - 50 and 150 mg tablets; L-PAM - 2 mg tablets; PRED - 5, 20 and 50 mg tablets; VCR - 1 and 5 mg ampules.

DATE SUMMARIZED: 11/79

5.0011 INDUCTION CHEMOTHERAPY WITH ADR/BCNU/CTX/VBL/PRED AND HIGH-DOSE CTX/VCR/PRED PLATEAU-PHASE MAINTENANCE FOR MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) BCRP-8001

OBJECTIVES:

I. Test feasibility of maximally tolerated Induction chemotherapy using adriamycin (ADR), vinblastine (VBL), BCNU, and cyclophosphamide (CTX) plus prednisone (PRED) in the setting of maximal supportive care for patients with multiple myeloma.

II. Test whether aggressive plateau-phase treatment with pulsed doses of cyclophosphamide, vincristine (VCR), and PRED might prolong remission.

III. Determine whether maximally tolerable Induction chemotherapy followed by aggressive plateau-phase treatment prolongs the survival of patients with myeloma compared to historical controls.

IV. Study the toxicities of these regimens and determine whether survival benefits warrant toxicity.

PROTOCOL ENTRY CRITERIA: Patients with previously treated or untreated, documented multiple myeloma; patients may have both multiple myeloma and amyloid disease. Prior therapy with corticosteroids, chemotherapeutic agents (other than adriamycin, nitrosoureas, or high-dose cyclophosphamide) and radiotherapy (provided the WBC count and platelet count are recovering from the nadir following irradiation) is acceptable. Patients may not have active congestive heart failure or cardiac arrythmias unless due to anemia.

PROTOCOL OUTLINE: Nonrandomized study. Enter previously untreated patients and previously treated, evaluable patients not in clinical remission to Induction therapy; those in clinical remission will be observed only.

Induction:

4-Drug Combination Chemotherapy plus Hormone Therapy. Adriamycin, ADR, NSC-123127; BCNU, NSC-409962; Cyclophosphamide, CTX, NSC-26271; Vinblastine, VBL, NSC-49842; plus Prednisone, PRED, NSC-10023.

Maintenance:

2-Drug Combination Chemotherapy plus Hormone Therapy. High-dose CTX; Vincristine, VCR, NSC-67574; PRED.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: HLA, lymphocytotoxic antibody, CBC, PLTS, WBC, SMA-6, SMA-12, LFT, serum protein immunoelectrophoresis, EKG, bone marrow aspirate/biopsy, coagulation profile.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, duration of response, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction:

PRED - 100 mg/sqm po on days 1, 5, and 28 through 32; VBL - 0.1 mg/kg iv on days 1 and 28; ADR - 45 mg/sqm iv push on days 1 and 28; BCNU - 100 mg/sqm iv infusion (drip) over 1 hour on day 1; CTX - 600 mg/sqm iv infusion (drip) over 2 hours on days 1 and 2, and 28 and 29. Repeat at 56-day intervals. The drugs must be administered in the sequence indicated and within 5-10 minutes after the end of the infusion of the preceding drug. Patients achieving a clinical remission-plateau phase should proceed to Maintenance only after a minimum of 3 courses, including one Induction course following remission. Patients continuing to show significant progressive marrow improvement with each Induction course will continue Induction therapy. Patients not achieving plateau phase after 6 Induction courses are considered failures.

Maintenance:

PRED - 100 mg/sqm po on days 1 through 5; VCR - 2 mg/sqm iv push on day 1; CTX - 2 g/sqm iv infusion (drip) over 4 hours on day 1. Repeat q 6 weeks for a total of 12 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; CTX - 100, 200, and 500 mg vials; PRED - 5, 10, and 20 mg tablets; VBL - 10 mg vials. ADR and VCR are not given.

DATE SUMMARIZED: 10/80

5.0012 CHEMOTHERAPY WITH INVESTIGATIONAL DRUGS AND L-PAM/PRED FOR UNRESPONSIVE MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) MDAR-274; MDA-MED-178

OBJECTIVES:

I. Determine the survival time and duration of a stable tumor mass in unresponsive patients with a low residual plasma cell population after 18 months of combination chemotherapy.

II. Compare these findings with those in unresponsive patients with a higher residual tumor mass who will receive investigational and/or melphalan (L-PAM) prednisone (PRED) therapies.

PROTOCOL ENTRY CRITERIA: Patients with multiple myeloma who have failed to achieve 75% reduction in tumor mass after 18 months of therapy on Protocol 7704.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with intermediate tumor mass and either unresponsive or with more than 50% reduction in tumor mass to Regimen A. Enter those with intermediate tumor mass who are either unresponsive or with less than 50% reduction in tumor mass to Regimens B or C.

Regimen A: No treatment.

Regimen B: Single-agent Chemotherapy. Investigational drug - highest priority Phase II SWOG protocol.

Regimen C: Single-agent Chemotherapy plus Hormone Therapy. Melphalan, L-PAM, NSC-8806; Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Survival time, duration of response.

CURRENT STATUS: About 40 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Regimen A: No treatment.

Regimen B: Investigational drug - no dosage details given.

Regimen C: L-PAM; PRED. No dosage details given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

5.0013 PHASE II EVALUATION OF VINDESINE IN THE TREATMENT OF REFRACTORY MULTIPLE MYELOMA IN ADULTS

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PROTOCOL NUMBER(S) MDAR-423; MDA-DT-8049

OBJECTIVES:

I. Evaluate the therapeutic efficacy of vindesine in patients with refractory multiple myeloma.

II. Determine the qualitative and quantitative toxicity of this treatment.

III. Evaluate the effect of vindesine on normal hemopoietic and myeloma tumor cells regarding the prediction of the degree of myelosuppression and tumor cell sensitivity, respectively.

PROTOCOL ENTRY CRITERIA: Adult multiple myeloma patients who are not candidates for known regimens or higher priority protocols. Patients must have a life expectancy of at least 12 weeks and may not have received chemotherapy within the 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: At least 14 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 2 mg/sqm iv bolus on days 1, 8, and 15. Repeat course q 6 weeks. When the WBC nadir is more than 2000 and the platelet nadir more than 100,000, escalate dose by 25 percent.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

5.0014 COMBINATION CHEMOTHERAPY WITH BCNU/CTX/L-PAM/VCR PLUS PREDNISONE FOR PROGRESSIVE GENERALIZED MYELOMA

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PROTOCOL NUMBER(S) MSKCC-7218B

OBJECTIVES:

I. Obtain longer objective and subjective remissions and prolong survival in multiple myeloma.

PROTOCOL ENTRY CRITERIA: Not given.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy plus Hormone Therapy. BCNU, NSC-409962; Cyclophosphamide, CTX, NSC-26271; Melphalan, L-PAM, NSC-8806; Vincristine, VCR, NSC-67574; plus Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

BCNU - 0.5 mg/kg iv on day 1; CTX - 10 mg/kg iv on day 1; L-PAM - 0.25 mg/kg po on days 1 through 4; VCR - 0.03 mg/kg iv on day 1; plus PRED - 1 mg/kg/day po on days 1 through 7, then 0.5 mg/kg for one week, then 0.25 mg/kg for 2 weeks, q other day for 2 weeks, or maintained as clinically necessary. Repeat course q 5 weeks for responders.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/78

5.0015 PHASE I-II STUDY OF TOTAL BODY IRRADIATION FOR MULTIPLE MYELOMA RESISTANT TO SYSTEMIC CHEMOTHERAPY

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PROTOCOL NUMBER(S) NCI-80-C-69

OBJECTIVES:

I. Determine the acute hematologic and other toxicities of total body irradiation (TBI) in patients with multiple myeloma who have progressed on prior chemotherapeutic regimens.

II. Assess the frequency and duration of subjective and objective improvement following TBI.

PROTOCOL ENTRY CRITERIA: Patients 30-70 years of age with an unequivocal histologic diagnosis of a malignant plasma cell dyscrasia, including multiple myeloma, Waldenstrom's macroglobulinemia, plasma cell leukemia, amyloidosis with M-protein. Patients must have failed initial cytotoxic chemotherapy including at least one alkylating agent (at least 2 cycles of melphalan, cyclophosphamide, or BCNU), and have a performance status of 3 or less (ECOG), an expected survival of at least 3 months, and at least fair renal status. There must be no evidence suggesting spinal cord compression, and hematologic parameters must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Total body irradiation (TBI) with 6 MeV linear accelerator.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hemogram, serum chemistries including electrolytes, renal function tests, serum protein electrophoresis, chest x-ray, bone marrow aspirate, quantitative serum immunoglobulins.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, subjective response.

CURRENT STATUS: 20 patients will be entered.

DOSAGE SCHEDULE:

TBI - 50 rads/week to a maximum of 200 rads or until hematologic suppression develops. In the absence of intolerable hematologic toxicity in the first 5 patients, escalate to 71 rads/week to a total of 300 rads in the subsequent 5 patients.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 08/80

5.0016 IMMUNOTHERAPY WITH INTERFERON FOR MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) NY-ACSCS-1

OBJECTIVES:

I. Evaluate the possible therapeutic usefulness of human leukocyte interferon (IF) in the treatment of patients with multiple myeloma.

PROTOCOL ENTRY CRITERIA: Patients with active, progressive myeloma with overt skeletal lesions, monoclonal gammopathy, marrow plasmacytosis, and anemia, with expected survival time of more than 6 months. Patients may not have hypercalcemia, azotemia not correctable by hydration, amyloidosis, nor have received radiotherapy less than 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy. Human Leukocyte Interferon, IF.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Serial determination of concentration of monoclonal serum immunoglobulins and urinary Bence-Jones protein; calcium balance; complete blood count.

END POINTS: Response/remission rate.

CURRENT STATUS: Up to 30 patients will be entered.

DOSAGE SCHEDULE:

Induction: IF - 3 x 10 to the sixth units/day im for 14 days. Dosage increased to 6 x 10 to the sixth units/day for 3 months in absence of granulocytopenia. Nonresponders will be withdrawn from treatment; slow responders continue for 3 additional months at either 3 or 6 x 10 to the sixth units dosage level.

Maintenance: Responders achieving remission after 3 or 6 months of therapy will receive IF for an additional 12 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: IF - 3 x 10 to the sixth units ampules.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

5.0017 COMBINATION CHEMOTHERAPY WITH L-PAM/PRED AND CTX/PRED OR CCNU/VCR/PRED/ADR MAINTENANCE FOR MULTIPLE MYELOMA

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PROTOCOL NUMBER(S) CAN-NCIC-MY2

OBJECTIVES:

I. Determine whether there is need for continuous chemotherapy in responsive, 'stable' cases of multiple myeloma when such a response had been induced by combined use of melphalan (L-PAM) and prednisone (PRED).

II. Determine whether cyclophosphamide (CTX) can induce remission in L-PAM/PRED resistant cases, and compare the remission induction rate with that obtained in similar cases treated with a combination of CCNU/vincristine (VCR)/adriamycin (ADR)/-PRED.

III. Determine whether this combination can induce a response in: a) cases resistant to the primary treatment with L-PAM/PRED combination. b) cases which have responded to L-PAM/PRED combination or CTX therapy, but who have subsequently relapsed - entered the 'accelerated phase'.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven plasma cell myeloma or solitary plasmacytona following Radiotherapy. Patients must have measurable serum or urine M-protein, adequate cardiac status and no prior therapy with alkylating agents.

PROTOCOL OUTLINE: Randomized study.

Induction: 2-Drug Combination Chemotherapy. Melphalan, L-PAM, NSC-8806; Prednisone, PRED, NSC-10023.

Arm I: No therapy.

Maintenance: 2-Drug Combination Chemotherapy. L-PAM, PRED.

Arm II: 2-Drug Combination Chemotherapy. PRED; Cyclophosphamide, CTX, NSC-26271.

Arm III: 3-Drug Combination Chemotherapy. PRED; Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127, or CCNU, NSC-79037.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Quantitative serume electrophoresis, 24-hour urine protein, SMA-18, immuno electrophoretic classification of M-protein.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of survival, duration of remission.

CURRENT STATUS: 350 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Induction: L-PAM - 9 mg/sqm (increase dose to 12 mg/sqm if tolerated) po on days 1 through 4; PRED - 100 mg in divided doses po on days 1 through 4. Repeat course q 4 weeks. Randomize patients in stable condition for 4 months to continued Induction therapy or Maintenance Arm I. Continue patients without change on L-PAM/PRED until disease is stable or progresses. Randomize patients with progressive disease after a minimum of 12 weeks to Arms II or III. Enter patients who relapse after reinduction to Arm III.

Maintenance:

Arm I: No therapy. Enter patients who relapse to reinduction with L-PAM/PRED.

Arm II: CTX - 325 mg/sqm po on days 1 through 4; PRED as in Induction. Repeat for at least 12 weeks, then enter patients with no change or progressive disease to Arm III. Continue responders on CTX/PRED until relapse, then enter them to Arm III.

Arm III: CCNU - 20 mg/sqm po on day 1; VCR - 0.6 mg/sqm (maximum dose 2.0 mg) iv on day 1; PRED - 100 mg po on days 1 through 4; ADR - 30 mg/sqm (maximum cumulative dose 400 mg/sqm) iv on day 1. Repeat course q 4 weeks. Treat patients who fail to respond after 12 weeks at the discretion of the investigator. Continue responders on this therapy until maximum dose of ADR is reached, then substitute CCNU - 60 mg/sqm po (escalating to 130 mg/sqm if tolerated). Treat patients who relapse at the discretion of the investigator.

Follow all patients until death or for at least 5 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

5B. HISTIOCYTOSIS

5.0018 PHASE III INDUCTION AND MAINTENANCE CHEMOTHERAPY WITH PRED/VBL/MTX/CTX AND MTX/CTX/6-MP FOR HISTIOCYTOSIS X IN CHILDREN

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PROTOCOL NUMBER(S) CCG-984

OBJECTIVES:

I. Determine whether multidrug induction and maintenance regimens will improve survival in the young high-risk patients and reduce sequelae in the long-term survivors.

II. Obtain comprehensive immunologic studies at diagnosis and at critical times during the course of the disease to (a) identify patients with primary immunodeficiency disorders which may simulate histiocytosis X, (b) determine whether patients with histiocytosis X less than 3 years of age have acquired defects in T and B lymphocyte function, and (c) ascertain if either stage of disease or survival of these young patients can be correlated with T and B lymphocyte function.

III. Collect clinical and histologic data so that patients may be staged in a prospective fashion into those with and without organ dysfunction and those with 'benign' or 'malignant' histology, and recommend more detailed pathologic studies to increase knowledge of the cellular infiltrates in various tissues.

PROTOCOL ENTRY CRITERIA: Previously untreated patients less than 15 years old with a histological diagnosis of histiocytosis or patients without recognized primary immunodeficiency but with equivocal immunoglobulin levels, PHA, percentage of T or B cells and with disorders diagnosed as probable malignant reticuloendotheliosis or erythrophagocytic lymphohistiocytosis.

PROTOCOL OUTLINE: Nonrandomized study. Enter all patients to Induction therapy. Enter complete (CR) or partial responders (PR) to Maintenance therapy.

Induction:

3-Drug Combination Chemotherapy plus Hormone Therapy. Prednisone, PRED, NSC-10023; Vinblastine, VBL, NSC-49842; Methotrexate, MTX, NSC-740; Cyclophosphamide, CTX, NSC-26271.

Maintenance:

3-Drug Combination Chemotherapy. 6-Mercaptopurine, 6-MP, NSC-755; MTX; CTX. Radiotherapy. Selectively enter patients for localized disease not controlled by Chemotherapy and treat with megavoltage equipment.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Immunological studies: surface markers evaluation, quantitative IGE levels, lymphocyte blastogenesis with PHA stimulation; T and B lymphocyte function; histological staging; liver function tests.

END POINTS: Response/remission rate, survival rate, objective tumor response, recurrence rate, survival time, quality of survival.

CURRENT STATUS: About 30 patients will be entered in about 5 years.

DOSAGE SCHEDULE:

Induction: 12-week course.

PRED - 40 mg/sqm/day po in 3 divided doses on days 1 through 42. Taper to discontinue over 2 weeks until day 56; VBL - 6.5 mg/sqm iv on day 1 and q 7 days for 12 weeks, increasing dosage to 7.0 mg/sqm on days 15 and 22, to 7.5 mg/sqm on day 29 and thereafter if adequate granulocyte count; MTX - 10 mg/sqm po on day 2 and q 7 days for 12 weeks; CTX - 100 mg/sqm po on day 4 and q 7 days for 12 weeks. For an adequate trial, continue therapy for at least 4 weeks. Enter CR or PR to Maintenance therapy.

Maintenance: 6-month course.

6-MP - 50 mg/sqm/day po; MTX - 10 mg/sqm po on day 1 q 7 days; CTX - 100 mg/sqm po on day 4 q 7 days. If above dosages are tolerated by PR, increase MTX and CTX every 14 days up to 20 mg/sqm and 200 mg/sqm respectively.

Repeat Induction therapy for patients with disease recurrence.

Radiotherapy: For local skeleton involvement. Give 600 rad megavoltage therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PRED - 5 and 20 mg tablets; VBL - 10 mg vials; MTX -2.5 mg tablets; CTX - 25 and 50 mg tablets; 6-MP - 50 mg tablets.

DATE SUMMARIZED: 05/79

5C. POLYCYTHEMIA VERA

5.0019 PHASE II CHEMOTHERAPY WITH HYDROXYUREA FOR POLYCYTHEMIA VERA

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PROTOCOL NUMBER(S) PVSG-8

OBJECTIVES:

I. Evaluate the efficacy of Hydroxyurea (HU) in patients of all ages with polycythemia vera who have active disease.

II. Assess the influence of HU upon the symptoms and signs of active disease and upon the abnormal hematological and biochemical manifestations of the panymyelosis that characterize this condition.

PROTOCOL ENTRY CRITERIA: Previously treated patients of any age with well-documented active polycythemia vera (PV) four months after the conclusion of any myelosuppressive radiation or chemotherapy. Rising hematocrit may be managed by phlebotomy during the waiting period. PV must be established by a combination of parameters as categorized by the PV major protocol.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Hydroxyurea, HU, NSC-32065.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Bone marrow needle biopsy aspirate; red cell mass; J-125 albumin measurement for plasma volume; serum folate, B-12 and unbound B-12 binding capacity; erythropoietin, serum electrophoresis, bone marrow karyotype, leukocyte alkaline phosphatase.

END POINTS: Response/remission rate.

CURRENT STATUS: 75 to 150 patients will be entered per year.

DOSAGE SCHEDULE:

Induction:

Phlebotomize all patients to a hematocrit of less than 50%. HU - 30 mg/kg/day po in 2 divided doses given q 12 hours for 7 days.

Maintenance:

HU - 15 mg/kg/day po if the wbc is not less than 3500/cumm and platelets not less than 100,000/cumm. Adjust dosage to maintain a normal hematocrit and platelet count. Give iron replacement only to iron deficient patients.

Evaluate all patients after 4 and 8 weeks of Maintenance therapy. Continue therapy for complete responders. Escalate dose for partial responders after 8 weeks, for nonresponders after 4 and 8 weeks. Stop therapy if wbc is below 3500/cumm, platelets below 100,000/cumm, restart therapy at half dosage upon recovery. Remove from study patients failing to achieve complete response after 2 episodes of unacceptable leukopenia and thrombocytopenia.

Dosage modifications for toxicity are given.

DOSAGE FORMS: HU - 500 mg capsules.

DATE SUMMARIZED: 10/79

PATIENT ACCRUAL: 00490579

5D. MYCOSIS FUNGOIDES

5.0020 PHASE II CHEMOTHERAPY WITH CTX/ADR/VCR/PRED/BLEO FOLLOWING RADIOTHERAPY FOR STAGE I MYCOSIS FUNGOIDES

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PROTOCOL NUMBER(S) SWOG-7622R

OBJECTIVES:

I. Study the effectiveness of combined electron beam therapy and adjuvant chemotherapy for patients with Stage I mycosis fungoides as evidenced by frequency of induction of complete remission, disease-free interval, and percentage of recurrence. (Objective revised, April 1979.)

II. Determine effectiveness of adjuvant chemotherapy on survival patterns.

III. Determine the value of staging laparotomy in the treatment of mycosis fungoides. (This objective not included in revised protocol, April 1979.)

PROTOCOL ENTRY CRITERIA: Patients with histologic diagnosis of Stage I and II mycosis fungoides, with measurable lesions. Patients with Sezary cells plus skin involvement only will be considered Stage I (Fuks classification). Patients must have absolute granulocyte count of 2,000 or greater and a platelet count of 100,000 or greater at time of entry.

PROTOCOL OUTLINE: Nonrandomized study. Enter all patients to Regimen A. Those with residual disease after Regimen A go off study and are eligible for SWOG-7713; those achieving complete remission are entered to Regimen B.

Regimen A: Radiotherapy. Total body electron beam irradiation.

Regimen B: 4-Drug Combination Chemotherapy plus Hormone Therapy. CHOP - BLEO: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; Bleomycin, BLEO, NSC-125066.

STRATIFICATION BY: Complete or incomplete response to electron beam radiotherapy.

SPECIAL STUDY PARAMETERS: Description of skin lesions, immunological tests, tomograms of mediastinum and adjacent lung if hilar nodes are involved, pulmonary function tests including carbon monoxide diffusion capacity, liver-spleen scan, gallium scan, bipedal lymphangiogram.

END POINTS: Response/remission rate, duration of response, objective tumor response.

CURRENT STATUS: All available patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Radiotherapy - electron beam (2.5-4.0 MeV) total body irradiation by Stanford technique. Give 3000-3500 rads over 40-60 days. Give orthovoltage boost to 'shadow areas' not to exceed 1500 rads over 5 dayys. Enter complete responders to Regimen B.

Regimen B: CTX - 700 mg/sqm iv on day 1 only; ADR - 50 mg/sqm on day 1 only; VCR - 1.4 mg/sqm on day 1 (maximum dose 2 mg); BLEO - 3 units/sqm iv on day 1; PRED - 100 mg/day po for 5 days. (Chemotherapy doses revised, April 1979.) Begin Chemotherapy following completion of electron beam therapy, boost therapy, and rest period of four weeks, if biopsy and aspirate are normal, white count is greater than 300,000 and platelet count is greater than 100,000. Repeat course q 21 days for a total of 8 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg capsules; VCR - 1 and 5 mg ampules; ADR - 10 mg ampules; BLEO - 15 mg vials; PRED - 5, 20, and 50 mg tablets.

DATE SUMMARIZED: 04/80

5E. OTHER HEMATOLOGIC MALIGNANCIES

5.0021 PHASE II CHEMOTHERAPY WITH HYDROXYUREA FOR POLYCYTHEMIA VERA, MYELOFIBROSIS AND PRIMARY THROMBOCYTOSIS

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PROTOCOL NUMBER(S) PVSG-12

OBJECTIVES:

I. Evaluate the efficacy of hydroxyurea in preventing and controlling the symptoms of thrombosis and bleeding with 1) the clinical entity primary thrombocythemia, 2) myelofibrosis-myeloid metaplasia with elevated platelet counts, and 3) unclassified myeloproliferative disease with elevated platelet counts.

PROTOCOL ENTRY CRITERIA: Symptomatic or asymptomatic patients with a platelet count of at least 1,000,000 on 2 separate determinations, who are under age 30 or who have had prior radiation or chemotherapy or who did not respond to prior P-32 or L-PAM therapy. Patients with platelet counts between 600,000 and 1,000,000 who are symptomatic or who have a prolonged bleeding time, or who have a hereditary bleeding disorder, or who are taking oral anticoagulants. All patients must also have marked megakaryocytic hyperplasia and abundant platelet clumps in bone marrow. They must not have the Philadelphia chromosome or increased red cell mass; there may have been no previous splenectomy or pre-existing cancer, nor may thrombocytosis be secondary to some identifiable course.

PROTOCOL OUTLINE: Nonrandomized study.

Induction and Maintenance:

Single-agent Chemotherapy. Hydroxyurea, HU, NSC-32065.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Leukocyte alkaline phosphatase, Coombs' test, bone marrow aspirate and needle biopsy, bone marrow karyotype, rbc mass and plasma volume, plasma iron and total iron binding capacity, serum folate, serum B-12 and unbound B-12 binding capacity, liver/spleen scan if liver not palpably enlarged

END POINTS: Response rate, toxicity/morbidity of treatment, development of acute leukemia.

CURRENT STATUS: 50 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Anti-aggregating agents may not be given concomitant with HU therapy.

Induction:

HU - 30 mg/kg/day po given as 2 divided doses q 12 hours in a fasting state for 7 days. If Hb is at least 10 gm %, wbc at least 3500/cumm and platelets at least 1,000,000/cumm, enter patients to maintenance.

Maintenance:

HU - 15 mg/kg/day po. Discontinue therapy if hematological parameters fall below maintenance entrance requirements. Continue therapy unless unacceptable toxicity develops, with dosage adjustments according to hematological status. Follow up patients q week, when stabilized q 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: HU - 500 mg capsules.

DATE SUMMARIZED: 10/79

PATIENT ACCRUAL: 00280579

5.0022 PHASE II STUDY OF CIS-PLATINUM FOR NON-HODGKIN'S HEMATOLOGIC MALIGNANCIES

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PROTOCOL NUMBER(S) MSKCC-7827

OBJECTIVES:

I. Determine effect of cis-platinum on non-Hodgkin's lymphoma, leukemias, and multiple myeloma.

PROTOCOL ENTRY CRITERIA: Patients with pathological diagnosis of non-Hodgkin's lymphoma (Rappaport/Memorial Hospital classification), leukemia (French-American-British classification) or multiple myeloma (standard criteria) who have a Karnofsky performance status above 50, normal auditory function, and a creatinine clearance of 60 or more. There must be measurable disease.

PROTOCOL OUTLINE: Nonrandomized study. Assign patients with wbc of 3500 or more and platelet count of 100,000 or more to Regimen A and patients with wbc of 2000 to 3500 and platelet count of 35,000 to 100,000 to lower dose Regimen B. Enter nonresponders in Regimens A and B to Regimen C.

Regimen A: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Regimen B: Single-agent Chemotherapy. CACP, low dose.

Regimen C: Single-agent Chemotherapy. CACP, high dose.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Lymphangiogram; bone and gallium scan; bone marrow aspirate and biopsy; audiogram; serum and urine paraprotein (multiple myeloma only).

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: CACP - 60 mg/sqm iv with hydration q 2 weeks. Reevaluate patients after q 2 courses. If after 2 courses there is no response or progression of disease and creatinine clearance remains 60 or more, consider Regimen C.

Regimen B: CACP - 30 mg/sqm iv administered and evaluated as in Regimen A. Cross over nonresponders to Regimens A or C.

Regimen C: CACP - 120 mg/sqm iv with prehydration and mannitol diuresis. Evaluate as in Regimen A.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/79

SECTION 6

LEUKEMIA

6A. ACUTE LYMPHOCYTIC, UNDIFFERENTIATED AND STEM CELL LEUKEMIA

CCG-082 PHASE II IMMUNOTHERAPY WITH STABILIZED POLY-IC FOR PREVIOUSLY TREATED CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA 6.0001
CCG-161 PHASE III THERAPY WITH VCR/L-ASP/MTX-IT/MTX/6-MP, PRED PLUS CNS RADIOTHERAPY FOR LOW-RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA 6.0002
CCG-162 PHASE III VCR/L-ASP/6-MP/ARA-C/ADR/CTX/MTX/MTX-IT, PRED, PLUS CNS RADIOTHERAPY FOR AVERAGE-RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA 6.0003
CCG-163 PHASE III VCR/L-ASP/6-MP/ARA-C/CTX/MTX/CF, PRED, PLUS CNS RADIOTHERAPY FOR HIGH-RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA 6.0004
CCG-171 PHASE III VCR/L-ASP/PRED REINDUCTION & VCR/MTX/L-ASP MAINTENANCE FOR CHILDHOOD ACUTE LYMPHOCYTIC OR UNDIFFERENTIATED LEUKEMIA .. 6.0005
CCG-181 REINDUCTION OF REMISSION FOLLOWING FIRST BONE MARROW RELAPSE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA 6.0006
CCG-191P TOTAL SANCTUARY VS CONVENTIONAL CNS TREATMENT FOR NEWLY DIAGNOSED ACUTE LYMPHOBLASTIC LEUKEMIA 6.0007
CCG-905 EVALUATION OF MAINTENANCE THERAPY AFTER LONG-TERM CHEMOTHERAPY FOR CHILDREN IN REMISSION FROM ACUTE LYMPHOCYTIC LEUKEMIA ... 6.0008
CLB-7611R NO THERAPY VS SHORT-TERM CHEMOTHERAPY FOLLOWING TERMINATION OF MAINTENANCE FOR PEDIATRIC ALL AFTER 3-YEAR CONTINUOUS COMPLETE REMISSION 6.0009
SEG-78ALL333 PHASE III MTX/PRED/VCR INDUCTION, CNS PROPHYLAXIS, CHOP AND 6-MP/MTX/VCR/PRED WITH OR WITHOUT ARA-C/CTX/MEPRDL/ADR FOR ALL ... 6.0010
SWOG-7606 PHASE III CHEMOTHERAPY WITH INTRAVENOUS VS INTRAMUSCULAR L-ASP PLUS VCR/PRED FOR ACUTE LYMPHOCYTIC LEUKEMIA IN CHILDREN 6.0011
SWOG-7623 RADIOTHERAPY, CHEMOTHERAPY WITH VCR/PRED/L-ASP/MTX/6-MP, CTX, ARA-C, DNM & HYDROCORTISONE FOR ACUTE CHILDHOOD LYMPHOCYTIC LEUKEMIA 6.0012
SWOG-7712 PHASE III INTRATHECAL MTX/ARA-C/HC/CF PLUS INDUCTION AND RADIOTHERAPY FOR FIRST CNS RELAPSE IN ACUTE LYMPHOCYTIC LEUKEMIA 6.0013
SWOG-7810 PHASE II CHEMOTHERAPY WITH ANGUIDINE FOR PEDIATRIC AND ADOLESCENT ACUTE LYMPHOBLASTIC LEUKEMIA IN RELAPSE 6.0014
SWOG-7834 PHASE III ARA-C/TG/COAP WITH VS WITHOUT VAP MAINTENANCE PLUS CNS THERAPY AFTER VAP REINDUCTION FOR FIRST-RELAPSE PEDIATRIC ALL 6.0015
SWOG-7837 PHASE III SYSTEMIC AND CNS THERAPY, WITH VCR, PRED, L-ASP, ADR, ARA-C, TG, MTX, CTX, HC, AND RADIATION FOR T-CELL ALL IN CHILDREN ... 6.0016

SWOG-7866 PILOT CONSOLIDATION, MAINTENANCE & CNS THERAPY WITH COMBINATIONS OF L-ASP, CTX, MTX, HC, ARA-C, 6-MP, PRED, ADR AND TG FOR PEDIATRIC ALL 6.0017
SWOG-7901 PHASE III RESCUE THERAPY FOR NON-CNS EXTRAMEDULLARY DISEASE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA 6.0018
SWOG-8001 PHASE III EVALUATION OF TWO COMBINATION CHEMOTHERAPY/HORMONE THERAPY REGIMENS FOR MAINTENANCE IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA 6.0019
BCRP-7508 PHASE III INDUCTION WITH MOAD (MTX/VCR/L-ASP/DM) PLUS 6-MP, ADR, ARA-C, AND TG FOR ADULT ACUTE LYMPHOCYTIC LEUKEMIA 6.0020
MDAR-201 COMBINATION CHEMOTHERAPY WITH PREDNISOLONE, VCR, AND L-ASP FOR REINDUCTION OF REMISSION IN ACUTE LYMPHOCYTIC LEUKEMIA IN CHILDREN 6.0021
MDAR-203 IMMUNOTHERAPY WITH C. PARVUM PLUS COMBINATION CHEMOTHERAPY WITH CHOPBLEO FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN ADULTS 6.0022
MDAR-250 INDUCTION AND MAINTENANCE WITH VINCRISTINE/PREDNISONE/METHOTREXATE FOR CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA 6.0023
MSKCC-7339 MULTIPLE-AGENT CHEMOTHERAPY FOR THE INDUCTION, CONSOLIDATION AND MAINTENANCE OF ADULT ACUTE LYMPHOBLASTIC LEUKEMIA 6.0024
SJCRH-R-7 CYCLIC COMBINATION CHEMOTHERAPY WITH ADR/VCR/PRED/6-MP/MTX FOR RECURRENT CHILDHOOD LYMPHOCYTIC LEUKEMIA 6.0025
SJCRH-R-8 COMBINATION CHEMOTHERAPY WITH VM-26/ARA-C VS VCR/CTX FOR MAINTENANCE OF SECOND HEMATOLOGIC REMISSIONS OF CHILDHOOD LYMPHOCYTIC LEUKEMIA 6.0026
SJCRH-TOT-105 TOTAL THERAPY OF CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA IN PATIENTS AT STANDARD RISK 6.0027
ARG-GATLA-1-LLA-79 PHASE III CHEMOTHERAPY, ENDOCRINE THERAPY & IMMUNOTHERAPY WITH VCR/DNM/PRED, MTX/DM, 6-MP/MTX, AND LEVAMISOLE IN ACUTE LYMPHOBLASTIC LEUKEMIA 6.0028
EORTC-58791 INDUCTION, CONSOLIDATION, AND MAINTENANCE MULTI-DRUG COMBINATION CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA 6.0029
UKM-MRC-UKALL-VI VCR/PRDL, CTX/VCR/ARA-C/MTX/PRDL, L-ASP/VCR/ADR VS VCR/PRDL, 6-MP/L-ASP/MTX/CF, BOTH FOLLOWED BY RADIOTHERAPY AND MAINTENANCE FOR ALL 6.0030

6B. ACUTE MYELOGENOUS AND OTHER ACUTE NON-LYMPHOCYTIC LEUKEMIAS

CCG-243 PHASE III REINDUCTION WITH ARA-C/DNM VS CYC/DNM & MAINTENANCE WITH ARA-C/CTX VS CYC/CTX FOR ACUTE NON-ALL/AUL LEUKEMIA 6.0031
CCG-251 PHASE III COMBINATION CHEMOTHERAPY (CYCLIC VS CONTINUOUS) VS BONE MARROW TRANSPLANTATION IN PEDIATRIC ACUTE NON-LYMPHOCYTIC LEUKEMIA 6.0032
CLB-7921 PHASE III INDUCTION WITH DNM/ARA-C/TG AND MAINTENANCE WITH DNM/ARA-C/TG/VCR/PRED FOR ACUTE MYELOCYTIC LEUKEMIA 6.0033
EST-1479 COMBINATION CHEMOTHERAPY WITH DNM/ARA-C/6-TG WITH OR WITHOUT CONSOLIDATION FOR ACUTE NON-LYMPHOCYTIC LEUKEMIA 6.0034
EST-4479 PHASE II CHEMOTHERAPY WITH VP-16 VS AMSA FOR PATIENTS WITH ACUTE NONLYMPHOCYTIC LEUKEMIA IN RELAPSE 6.0035
NCOG-P-9L81 COMBINATION CHEMOTHERAPY WITH ARA-C/TG OR ARA-C/TG/DNM FOR ADULT ACUTE NONLYMPHOCYTIC LEUKEMIAS 6.0036
NCOG-9L62 CHEMOTHERAPY WITH AZC/TG FOR REFRACTORY ADULT ACUTE NONLYMPHOCYTIC LEUKEMIA (ANLL) 6.0037
NCOG-9L83 PHASE II CHEMOTHERAPY WITH AMSA FOR ACUTE NONLYMPHOCYTIC LEUKEMIAS REFRACTORY TO STANDARD THERAPY 6.0038

SEG-AML-P30	PHASE II PILOT CHEMOTHERAPY WITH VINBLASTINE FOR REFRACTORY ACUTE MYELOGENOUS LEUKEMIA	6.0039
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SEG-77AML0103	PHASE III THERAPY WITH DNM, ARA-C, AZC, BETA-TGDR, TG & BCG FOR INDUCTION, CONSOLIDATION & MAINTENANCE OF ACUTE MYELOGENOUS LEUKEMIA	6.0041
SWOG-8063	PHASE II-PILOT CHEMOTHERAPY WITH ANGUIDINE FOR ACUTE NONLYMPHOCYTIC LEUKEMIA REFRACTORY TO STANDARD THERAPY	6.0042
BCRP-7802	ARA-C/TG MAINTENANCE WITH/WITHOUT SPLENECTOMY OR ALLOGENEIC MYELOBLASTS AFTER DNM/ARA-C INDUCTION FOR ACUTE NONLYMPHOCYTIC LEUKEMIA	6.0043
BCRP-7810	PHASE II CHEMOTHERAPY WITH AMSA FOR PREVIOUSLY TREATED ACUTE NONLYMPHOCYTIC LEUKEMIA	6.0044
MDAR-239	LATE INTENSIFICATION WITH CROP (CTX/RBD/VCR/PRED) WITH OR WITHOUT ACTIVE SPECIFIC IMMUNOTHERAPY FOR AML	6.0045
MDAR-251	ADOAP INDUCTION PLUS ARA-C/TG MAINTENANCE IN PEPA WITH WBC TRANSFUSIONS FOR ADULT ACUTE MYELOGENOUS LEUKEMIA	6.0046
SJCRH-AML-R	TREATMENT OF RELAPSED CHILDHOOD ACUTE NONLYMPHOCYTIC LEUKEMIA WITH HIGH-DOSE MTX AND LEUCOVORIN RESCUE FOLLOWED BY AMSA	6.0047
SJCRH-AML-80	INTENSIVE SEQUENTIAL ADR/ARA-C, VP-16/AZC, 6-TG/ARA-C, AND ADR/ARA-C AFTER INDUCTION WITH DNM/ARA-C FOR CHILDHOOD ACUTE NONLYMPHOCYTIC LEUKEMIA	6.0048
UCLA-ALP-3	CHEMOTHERAPY WITH TAD (6-TG/ARA-C/DNM), ADR, AZC PLUS IMMUNOTHERAPY WITH C. PARVUM, ALLOGENEIC LEUKEMIC BLASTS FOR ACUTE MYELOGENOUS LEUKEMIA	6.0049
EORTC-LAM-2	CHEMOTHERAPY WITH ARA-C VS ARA-C/TG VS ARA-C/DNM FOR INDUCTION AND METHYL GAG OR ARA-C FOR MAINTENANCE IN ACUTE MYELOBLASTIC LEUKEMIA	6.0050
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EORTC-LAM-4	PHASE II-III CHEMOTHERAPY WITH ADR/VCR/ARA-C PLUS IMMUNOTHERAPY WITH BCG AND IRRADIATED CELLS FOR ACUTE MYELOGENOUS LEUKEMIA	6.0052
EORTC-06781	COMPARISON OF MAINTENANCE COMBINATIONS FOLLOWING ADR/VCR/ARA-C INDUCTION FOR AML	6.0053
ISR-ANLL-1	COMBINATION CHEMOTHERAPY WITH ARA-C/DNM/TG PLUS IMMUNOTHERAPY WITH MER-BCG FOR ACUTE NONLYMPHOCYTIC LEUKEMIA	6.0054
ITA-AIL-7801	CHEMOTHERAPY WITH ARA-C/DRB/TG, ARA-C/VCR/ADR, AND DRB/ARA-C/TG/VCR/DMX WITH OR WITHOUT BCG IMMUNOTHERAPY FOR AML	6.0055
JAP-ANLL-N-CWS-2	PHASE II MAINTENANCE CHEMOTHERAPY WITH AND WITHOUT IMMUNOTHERAPY WITH NOCARDIA RUBRA-CWS WITH AND WITHOUT ALLOGENEIC LEUKEMIA CELLS FOR ANLL	6.0056
SAFR-ANLL-1	COMBINATION CHEMOTHERAPY WITH OR WITHOUT BONE MARROW TRANSPLANT AND LONG-TERM VS SHORT-TERM MAINTENANCE IN ANLL	6.0057
SAFR-CT-LEU-2	BONE MARROW TRANSPLANTATION PLUS CYCLOSPORIN-A FOR ADULT ACUTE LEUKEMIA IN REMISSION	6.0058
SWE-LCS-AML-1	CHEMOTHERAPY PLUS BCG IMMUNOTHERAPY WITH OR WITHOUT ALLOGENEIC TUMOR CELLS FOR ACUTE MYELOID LEUKEMIA	6.0059
SWE-LCS-780901	COMBINATION CHEMOTHERAPY WITH ARA-C/DRB VS ARA-C/DRB-DNA COMPLEX FOR ACUTE NONLYMPHOCYTIC LEUKEMIA	6.0060
UKM-UHW-CAR-3	INDUCTION & MAINTENANCE CHEMOTHERAPY WITH ADR/ARA-C/6-TG VS CHEMO/IMMUNOTHERAPY ADR/ARA-C/6-TG PLUS BCG IN ACUTE MYELOGENOUS LEUKEMIA	6.0061

6C. CHRONIC LEUKEMIA

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6D. LEUKEMIA—GENERAL

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SEG-RAL-P38R PHASE I-II PILOT CHEMOTHERAPY WITH M-AMSA FOR REFRACTORY ACUTE LEUKEMIA 6.0077
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SWOG-7970 PHASE II CHEMOTHERAPY WITH AMSA FOR ACUTE LEUKEMIA 6.0083
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BCRP-7317 EVALUATION OF AUTOLOGOUS PLATELETS IN SUPPORTIVE CARE OF PATIENTS WITH ACUTE LEUKEMIA 6.0085
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MDAR-279 CONTINUOUS INFUSION CHEMOTHERAPY WITH ADRIAMYCIN FOR ACUTE LEUKEMIA 6.0090

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MDAR-285 PHASE II CHEMOTHERAPY WITH DEAZAURIDINE FOR ACUTE MYELOGENOUS OR LYMPHOCYTIC LEUKEMIA 6.0092

MDAR-291 CROPAM INDUCTION CHEMOTHERAPY AND ARA-C/TG CONSOLIDATION WITH OR WITHOUT BONE MARROW RESCUE FOR ALL, AUL, AND LYMPHOMA CELL LEUKEMIA 6.0093

MDAR-307 PHASE II CONTINUOUS INFUSION CHEMOTHERAPY WITH VINDESINE FOR ACUTE LEUKEMIA AND CHRONIC MYELOGENOUS LEUKEMIA IN BLAST CRISIS 6.0094

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MDAR-381 INDIVIDUALIZED CHEMOTHERAPY OF ADULT ACUTE LEUKEMIA BASED ON PREDICTED OUTCOME TO REMISSION INDUCTION AND MAINTENANCE TREATMENT 6.0097

MDAR-399 SURGERY AND/OR CHEMOTHERAPY WITH DRB AND/OR IMMUNOTHERAPY WITH MER AND MONONUCLEAR CELL TRANSFUSIONS FOR HAIRY CELL LEUKEMIA 6.0098

MDAR-411 PHASE I-II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR ACUTE LEUKEMIA 6.0099

MDAR-414 BONE MARROW RESTORATION WITH LITHIUM CARBONATE AND MER-BCG FOR OLIGOLEUKEMIA AND PRE-LEUKEMIA 6.0100

MDAR-415 HIGH-DOSE COMBINATION CHEMOTHERAPY WITH CTX/BCNU/VP-16 PLUS AUTOLOGOUS BONE MARROW TRANSPLANTATION FOR LEUKEMIA IN RELAPSE .. 6.0101

MDAR-416 CHEMOTHERAPY WITH PZD/MTX PLUS RADIOTHERAPY PLUS BONE MARROW TRANSPLANTATION FOR ADULT ACUTE LEUKEMIA IN REMISSION 6.0102

UCLA-BMT-40 BONE MARROW TRANSPLANTATION VS CHEMOTHERAPY WITH CTX PLUS RADIOTHERAPY FOR LEUKEMIA 6.0103

UTENN-LEU-1 IMMUNOTHERAPY WITH IMMUNE GAMMA GLOBULIN (LEUKOGLOBULIN) ALONE AND WITH SINGLE-AGENT CHEMOTHERAPY (DNM, MTX, CLB OR VCR) FOR LEUKEMIA 6.0104

CAN-NCIC-IC1 INDUCTION CHEMOTHERAPY AND ANTIBIOTIC THERAPY WITH AND WITHOUT LITHIUM CARBONATE FOR ACUTE LEUKEMIA 6.0105

JAP-KLSG-1 INDUCTION CHEMOTHERAPY WITH DCMP (DRB/ARA-C/6-MP/PRDL) OR VP (VCR/PRDL) PLUS MAINTENANCE WITH ARA-C/6-MP WITH OR WITHOUT LEV FOR ACUTE LEUKEMIA 6.0106

SAFR-CT-LEU-1 C. PARVUM IMMUNOTHERAPY FOR MAINTENANCE OF PATIENTS WITH ACUTE NONLYMPHOBLASTIC LEUKEMIA IN COMPLETE REMISSION 6.0107

SECTION 6

LEUKEMIA

6A. ACUTE LYMPHOCYTIC, UNDIFFERENTIATED AND STEM CELL LEUKEMIA

6.0001 PHASE II IMMUNOTHERAPY WITH STABILIZED POLY-IC FOR PREVIOUSLY TREATED CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-082

OBJECTIVES:

I. Determine therapeutic effectiveness of Poly/ICLC stabilized with poly-L-lysine and carboxymethyl cellulose in patients with acute lymphoblastic leukemia who have failed all standard drug therapy.

II. Correlate the effect of Poly-IC with interferon production, induction of autoimmune disease, lymphocyte subpopulations and monocyte function.

III. Correlate the efficacy of Poly-IC with type of acute lymphoblastic leukemia.

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age with acute lymphoblastic or acute myelocytic (CCG Report October 1979) leukemia who are in relapse after treatment with standard chemotherapy and higher priority investigational chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction and Maintenance:

Single-agent Immunotherapy. Poly-IC, NSC-120949.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, kidney and liver function studies. IEPA and IgE, serum interferon, cell surface markers, optional immune system studies.

END POINTS: Response, remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: As of 10/80, 22 patients have been entered.

DOSAGE SCHEDULE:

Induction:

Poly ICLC - 12 mg/sqm/day (reduced to 3 mg/sqm/day, CG Committee Report, October 1979) iv given over 1 hour for 14 days. Repeat course q 21 days for a minimum of 2 courses. If marrow is M1 on days 21 or 42 or M2 on day 42, start maintenance. If marrow is M3 on day 42, remove patient from study.

Maintenance:

Poly ICLC - 12 mg/sqm/day iv on days 1 through 7 q 28 days. Continue therapy until M3 marrow or development of unacceptable toxicity.

DOSAGE FORMS: Not given.

Dosage modifications for toxicity are not given.

DATE SUMMARIZED: 10/79

PATIENT ACCRUAL: 00101079

6.0002 PHASE III THERAPY WITH VCR/L-ASP/MTX-IT/MTX/6-MP, PRED PLUS CNS RADIOTHERAPY FOR LOW-RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) CCG-161

OBJECTIVES:

I. Evaluate the need of cranial irradiation for CNS prophylaxis by comparing the efficacy of cranial irradiation plus intrathecal methotrexate (MTX-IT) vs. MTX-IT plus maintenance MTX-IT.

II. Evaluate monthly vincristine (VCR) and prednisone (PRED) therapy in maintenance.

III. Evaluate the prognostic significance of surface marker analysis (E-rosette formation and surface immunoglobulins) of leukemic blast cells at diagnosis and relapse.

IV. Determine the effect of total drug dose/sqm/unit time on remission duration and survival.

V. Analyze patients who relapse or die in remission for features such as intercurrent illness, deviations and lapses in therapy, and cell surface markers in an attempt to better define prognostic groups and reasons for treatment failure.

PROTOCOL ENTRY CRITERIA: Patients 3 to 6 years of age with previously untreated acute lymphoblastic or undifferentiated (peroxidase and Sudan black negative) leukemia (not Burkitt's) with initial wbc of less than 10,000. Enter patients with pure L-2 or L2/L1 morphology to protocol CCG-162 (Addendum 3, November 1978).

PROTOCOL OUTLINE: Randomized study for Intensification and Maintenance only. Enter all patients to Induction.

Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; L-Asparaginase, L-ASP, NSC-109229; Methotrexate intrathecally, MTX-IT, NSC-740; plus Prednisone, PRED, NSC-10023.

Intensification: Randomize to Arm I or II, all patients who on day 28 of Induction have MI (0-5% blast cells) or M2 (6-25% blast cells) bone marrow rating, peripheral absolute neutrophil count greater than 1,000, and platelet count greater than 100,000.

Arm I: 2-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. MTX-IT; 6-Mercaptopurine, 6-MP, NSC-755; plus PRED; plus supervoltage radiation with Co-60, 4 and 6 MeV Linacs or higher photon energies to 10 MeV to entire calvarium.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. MTX-IT; 6-MP; plus PRED.

Maintenance: Randomize patients who on day 56 have above qualifications for entering Intensification from Arm I to Arm IIIA or B and from Arm II to Arm IVA or B.

Arm IIIA: 2-Drug Combination Chemotherapy. MTX; 6-MP.

Arm IIIB: 3-Drug Combination Chemotherapy plus Hormone Therapy. MTX; 6-MP; VCR; plus PRED.

Arm IVA: 2-Drug Combination Chemotherapy. MTX; 6-MP; and MTX-IT.

Arm IVB: 3-Drug Combination Chemotherapy plus Hormone Therapy. MTX; 6-MP; VCR; and MTX-IT; plus PRED.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Head circumference; accurate measurement of hepatomegaly, splenomegaly, lymphadenopathy, kidney and gonadal abnormalities; bone marrow histochemistry (peroxidase and Sudan black), morphology, and cell surface markers; IVP if serum creatinine is elevated; lumbar puncture; wrist X-ray; pubertal status; varicella antibody titers; and serum immunoglobulins.

END POINTS: Toxicity/morbidity of treatment, duration of remission, survival rate, response/remission rate, immunologic competence, survival time.

CURRENT STATUS: 330 patients will be entered in three years.

DOSAGE SCHEDULE:

Induction (days 0 through 28): VCR - 1.5 mg/sqm (maximum dose 2 mg) iv q 7 days; L-ASP - 6,000 IU/sqm im 3 times a week for 3 weeks starting on day 3; MTX-IT - 12 mg intrathecally (it) on days 0 and 14; PRED - 40 mg/sqm/day po in 3 divided doses. Remove patients with M3 bone marrow on day 28 from study.

Intensification (days 28 through 56):

Arm I: Ml marrow on day 28: MTX-IT - 12 mg q week starting on day 28 for 4 weeks; 6-MP - 75 mg/sqm/day po starting on day 28; PRED - 40 mg/sqm po starting on 28 and tapered to 0 in 14 days; 1800 rad in 10 treatments (5 days/week) starting on day 28 to entire calvarium and brain stem to level of C2 plus 1200 rad to unresolved persistent mass lesions. M2 marrow on day 28: MTX-IT, 6-MP, cranial irradiation, and treatment of persistent masses - as for M1 marrow; PRED - 40 mg/sqm/day po in 3 divided doses on days 28 through 42, then taper over 14 days to 0; VCR - 1.5 mg/sqm iv q 7 days for 2 weeks starting on day 35.

Arm II: M1 marrow on day 28: MTX-IT, 6-MP, PRED, treatment of persistent masses, as in Arm I. M2 marrow on day 28: MTX-IT, 6-MP, VCR, PRED, treatment of persistent masses - as in Arm I.

Maintenance: For Arms IIIA and B, IVA and B: Day 56 is day 0 of first Maintenance cycle. Repeat 84-day cycle for 12 courses, then discontinue therapy for patients in complete remission. Day 84 of one cycle is day 0 of next (84/0). All doses begin on day 84/0 of each cycle unless otherwise noted. Recalculate dose at beginning of every cycle to adjust to increases in body surface.

Arm IIIA: MTX - 20 mg/sqm po q week; 6-MP - 75 mg/sqm/day po.

Arm IIIB: MTX, 6-MP - as in Arm IIIA; VCR - 1.5 mg/sqm iv q 28 days; PRED - 40 mg/sqm po in 3 divided doses on days 1 through 5 q 28 days.

Arm IVA: 6-MP - as in Arm IIIA; MTX - 20 mg/sqm po q week beginning on day 7; MTX-IT - 12 mg it on day 84/0 (omit oral MTX on day of MTX-IT).

Arm IVB: 6-MP, MTX, MTX-IT - as in Arm IVA; VCR, PRED - as in Arm IIIB.

Remove patients with M3 bone marrow anytime during Intensification, Maintenance or Observation from study. Modifications are given for CNS leukemia at diagnosis and CNS leukemia or other extramedullary relapse during marrow remission.

Addendum, July 1980. Patients in bone marrow relapse while on therapy go off study. Patients in bone marrow relapse while off therapy remain on study and are reinduced with Induction/Intensification/Maintenance arm originally received, cranial irradiation excepted.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-ASP - 10,000 IU vials; PRED - 5 mg tablets; VCR - 1 and 5 mg vials; MTX - 5 and 50 mg vials, 2.5 mg tablets; 6-MP - 50 mg tablets.

DATE SUMMARIZED: 02/79

PATIENT ACCRUAL: 00720279

6.0003 PHASE III VCR/L-ASP/6-MP/ARA-C/ADR/CTX/MTX/MTX-IT, PRED, PLUS CNS RADIOTHERAPY FOR AVERAGE-RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America

PROTOCOL NUMBER(S) CCG-162

OBJECTIVES:

I. Evaluate the effect of the addition of monthly pulse doses of cyclophosphamide (CTX)/adriamycin (ADR)/cytosine arabinoside (ARA-C) to standard maintenance therapy.

II. Evaluate the effect of periodic reinduction with vincristine (VCR)/prednisone (PRED)/L-asparaginase (L-ASP).

III. Evaluate the addition of IT methotrexate (MTX-IT) during maintenance relative to control of CNS leukemia and marrow relapse.

IV. Evaluate the prognostic significance of surface marker analysis (E-rosette formation and surface immunoglobulins) of leukemic blast cells at diagnosis and relapse.

V. Determine the effect of total drug dose/sqm/unit time on remission duration and survival.

VI. Analyze patients who relapse or die in remission for features such as intercurrent illness, deviations and lapses in therapy, and cell surface markers in an attempt to better define prognostic groups and reasons for treatment failure.

PROTOCOL ENTRY CRITERIA: Patients with previously untreated acute lymphoblastic or undifferentiated leukemia (not Burkitt's) ages 3 to 6 years with initial wbc between 10,000 and 50,000 or under 3 years or 7 to 20 years old with a wbc of less than 50,000.

PROTOCOL OUTLINE: Randomized study for Maintenance only. Enter all patients to Induction.

Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; L-Asparaginase, L-ASP, NSC-109229; Methotrexate intrathecal, MTX-IT, NSC-740; plus Prednisone, PRED, NSC-10023.

Intensification: Enter all patients who on day 28 of Induction have M1 or M2 bone marrow, peripheral absolute neutrophil count greater than 1,000, and platelet count greater than 100,000. 2-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. 6-Mercaptopurine, 6-MP, NSC-755; MTX-IT; plus PRED; plus supervoltage radiation with Co-60, 4 and 6 MeV Linacs, or higher photon energies to 10 MeV to entire calvarium.

Maintenance: Randomize to Arms I or II patients who on day 56 have above qualifications for entering Intensification.

Arm I: Randomize patients in Arm I to Arm IA, IB or IC.

Arm IA: Standard Maintenance: 3-Drug Combination Chemotherapy plus Hormone Therapy. 6-MP; MTX; VCR; plus PRED.

Arm IB: Additive Maintenance: 6-Drug Combination Chemotherapy plus Hormone Therapy. 6-MP; MTX; VCR; Cytosine Arabinoside, ARA-C, NSC-63878; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; plus PRED.

Arm IC: Reinduction Maintenance: 4-Drug Combination Chemotherapy plus Hormone Therapy. 6-MP; MTX; VCR; L-ASP; plus PRED.

Arm II: Randomize patients in Arm II to Arms IIA, IIB, or IIC. Arms IIA, IIB and IIC are the same as Arms IA, IB, and IC respectively except that MTX-IT is substituted for MTX in each one.

STRATIFICATION BY: Participating institutions, age.

SPECIAL STUDY PARAMETERS: Head circumference; accurate measurement of hepatomegaly, splenomegaly, lymphadenopathy, kidney and gonadal abnormalities; bone marrow histochemistry (peroxidase and Sudan black), morphology, and cell surface markers; IVP if serum creatinine is elevated; lumbar puncture, wrist X-ray; pubertal status; varicella antibody titers; and serum immunoglobulins.

END POINTS: Toxicity/morbidity of treatment, duration of remission, survival rate, response/remission rate, immunologic competence, survival time.

CURRENT STATUS: 680 patients will be entered in three years.

DOSAGE SCHEDULE:

Induction (days 0 through 28): VCR 1.5 mg/sqm (maximum single dose 2 mg) q 7 days starting on day 0; L-ASP - 6000 IU/sqm im 3 times a week for 3 weeks starting on day 3; MTX-IT - 6 mg (less than age 1), 8 mg (age 1 to 2), 10 mg (age 2 to 3), 12 mg (age 3 and above) on days 0 and 14; PRED - 40 mg/sqm/day po in 3 divided doses. Remove patients with M3 bone marrow on day 28 from study.

Intensification (days 28 through 56): M1 bone marrow on day 28: MTX-IT - as in Induction on day 0 or q week for 4 weeks starting on day 28; 6-MP - 75 mg/sqm/day po starting on day 28; PRED - 40 mg/sqm po on day 28 and tapering to 0 by day 42; 1800 rad in 10 treatments (5 days/week) to entire calvarium and brain stem to level of C2 starting on day 28 plus 1200 rad to unresolved persistent mass lessions. M2 bone marrow on day 28: MTX-IT, PRED, and cranial irradiation - as for M1 marrow; VCR - 1.5 mg/sqm iv on days 35 and 42; Pred - 40 mg/sqm/day po in 3 divided doses on days 28 through 42, then taper over 14 days to 0.

Maintenance: For all Arms: Day 56 is day 0 or first Maintenance cycle. Repeat 84 day cycle for 12 courses, then discontinue therapy for patients in complete remission. Day 84 of one cycle is day 0 of next (84/0). All doses begin on day 84/0 of each cycle unless otherwise noted. Recalculate dose at beginning of every cycle to adjust to increases in body surface.

Arm IA: 6-MP - 75 mg/sqm/day po; MTX - 20 mg/sqm po q week; VCR -1.5 mg/sqm iv q 28 days; PRED - 40 mg/sqm po in 3 divided doses on days 1 through 5 q 28 days.

Arm IB: 6-MP, MTX, VCR, and PRED - as in Arm IA; ARA-C - 75 mg/sqm im, iv or sc on days 0 through 3; CTX - 30 mg/kg (900 mg/sqm) iv over 1 to 2 hours on day 28; ADR - 30 mg/sqm iv on day 56.

Arm IC: Cycles 1, 3, 5, 7, 9, and 11: 6-MP, MTX - as in Arm IA. Cycles 2, 4, 6, 8, 10 and 12: PRED - 40 mg/sqm/day po in 3 divided doses on days 0 through 28, then taper to 0 over 14 days; VCR - 1.5 mg/sqm iv q 7 days; L-ASP - 6000 IU/sqm im 3 times a week starting on day 3; 6-MP - 75 mg/sqm/day po; MTX - 20 mg/sqm po q week starting on day 35.

Arm IIA: 6-MP, MTX, VCR, PRED - as in Arm IA except begin MTX on day 7; MTX-IT - as in Induction on day 84/0.

Arm IIB: 6-MP, MTX, VCR, PRED, MTX-IT - as in Arm IIA; ARA-C, CTX, ADR - as in Arm IB.

Arm IIC: 6-MP, MTX, VCR, L-ASP, PRED - as in Arm IC except begin oral MTX on day 7; MTX-IT - as in Arm IIA.

Remove patients with M3 bone marrow anytime during Intensification, Maintenance or Observation from study. Modifications are given for CNS leukemia at diagnosis and CNS leukemia or other extramedullary relapse during marrow remission.

Addendum, July 1980. Patients in bone marrow relapse while on therapy go off study. Patients in bone marrow relapse while off therapy remain on study and are reinduced with Induction/Intensification/Maintenance arm originally received, cranial irradiation excepted.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-ASP - 10,000 IU vials; PRED - 5 mg tablets; VCR -1 and 5 mg vials; MTX - 5 and 50 mg vials and 2.5 mg tablets; 6-MP - 50 mg tablets; CTX - 100, 200 and 500 mg vials; ADR - 10 mg vials; ARA-C - 100 and 500 mg vials.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 02030279

6.0004 PHASE III VCR/L-ASP/6-MP/ARA-C/CTX/MTX/CF, PRED, PLUS CNS RADIOTHERAPY FOR HIGH-RISK CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) CCG-163

OBJECTIVES:

I. Determine effect of addition of IT methotrexate (MTX-IT) during maintenance to cranial radiation and MTX-IT for CNS prophylaxis.

II. Compare the addition of monthly pulse doses of cytosine arabinoside (ARA-C), cyclophosphamide (CTX), and adriamycin (ADR) to standard maintenance therapy vs. repeated cyclic courses of POMP, COP, POCA and MTX-IT with citrovorum rescue (CF).

III. Evaluate the prognostic significance of surface marker analysis (E-rosette formation and surface immunoglobulins) of leukemia blast cells at diagnosis and relapse.

IV. Determine the effect of total drug dose/sqm/unit time on remission duration and survival.

V. Study patients who relapse or die in remission for intercurrent illness, deviations and lapses in therapy and the relationship of these events to extramedullary disease.

PROTOCOL ENTRY CRITERIA: Patients less than 21 years of age with untreated acute lymphocytic or undifferentiated leukemia (not Burkitt's) who have an initial wbc of more than 50,000.

PROTOCOL OUTLINE: Randomized study for Maintenance only. Enter all patients to Induction.

Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; L-Asparaginase, L-ASP, NSC-109229; Methotrexate intrathecal, MTX-IT, NSC-740; plus Prednisone, PRED, NSC-10023.

Intensification: Enter all patients who on day 28 of Induction have M1 or M2 bone marrow, peripheral absolute neutrophil count greater than 1,000, and platelet count greater than 100,000. 2-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. 6-Mercaptopurine, 6-MP, NSC-755; MTX-IT; plus PRED; plus supervoltage radiation with Co-60, 4 and 6 MeV Linacs or higher photon energies to 10 MeV to entire calvarium.

Maintenance: Randomize to Arms I or II patients who on day 56 have above qualifications for entering Intensification.

Arm I: 6-Drug Combination Chemotherapy plus Hormone Therapy. 6-MP; MTX; MTX-IT; VCR; Cytosine Arabinoside, ARA-C, NSC-63878; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; plus PRED.

Arm II: 7-Drug Combination Chemotherapy plus Hormone Therapy. POMP: 6-MP, MTX, plus MTX-IT, PRED; followed by COP: VCR, CTX, PRED; followed by POCA: VCR, PRED, ADR, ARA-C; followed by MTX plus Citrovorum factor, CF, NSC-3490.

STRATIFICATION BY: Participating institutions, sex.

SPECIAL STUDY PARAMETERS: Head circumference; accurate measurement of hepatomegaly, splenomegaly, lymphadenopathy, kidney and gonadal abnormalities; bone marrow histochemistry (peroxidase and Sudan black), morphology, and cell surface markers; IVP if serum creatinine is elevated; lumbar puncture; wrist x-ray; pubertal status; varicella antibody titers; and serum immunoglobulins.

END POINTS: Toxicity/morbidity of treatment, duration of remission, survival rate, response/remission rate, immunologic competence, survival time.

CURRENT STATUS: 230 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Induction (days 0 through 28): VCR - 1.5 mg/sqm (maximum single dose 2 mg) q 7 days starting on day 0; L-ASP - 6000 IU/sqm im 3 times a week for 3 weeks starting on day 4; MTX-IT - 6 mg (less than age 1), 8 mg (age 1 to 2), 10 mg (age 2 to 3), 12 mg (age 3 and above) on days 0 and 14; PRED - 40 mg/sqm/day po in 3 divided doses. Remove patients with M3 bone marrow on day 28 from study.

Intensification (days 28 through 56): M1 bone marrow on day 28: MTX-IT - as in Induction on day 0 of q week for 4 weeks starting on day 28; 6-MP - 75 mg/sqm/day po starting on day 28; PRED - 40 mg/sqm po on day 28 and tapering to 0 by day 42; 1800 rad in 10 treatments (5 days/week) to entire calvarium and brain stem to level of C2 starting on day 28 plus 1200 rad to unresolved persistent mass lesions. M2 bone marrow on day 28: MTX-IT, PRED, and cranial irradiation - as for M1 bone marrow; VCR - 1.5 mg/sqm iv on days 35 and 42; PRED - 40 mg/sqm/day po in 3 divided doses on days 28 through 42, then taper over 14 days to 0.

Maintenance: For both Arms I and II: Day 56 is day 0 of the first Maintenance cycle. Repeat 84 day cycle for 12 courses, then discontinue therapy for patients in complete remission. Day 84 of one cycle is day 0 of next (84/0). All doses begin on day 84/0 of each cycle unless otherwise noted. Recalculate dose at beginning of each cycle to adjust for increases in body surface.

Arm I: 6-MP - 75 mg/sqm/day po; MTX - 20 mg/sqm po q week beginning on day 7; VCR - 1.5 mg/sqm (maximum daily dose 2 mg) iv on days 84/0, 28, 56; PRED - 40 mg/sqm/day po in 3 divided doses for 5 days starting on day 84/0, 28 and 56; ARA-C - 75 mg/sqm im, iv or sc on days 84/0 through 3; CTX - 30 mg/kg (900 mg/sqm) iv over 1 to 2 hours on day 28; ADR - 30 mg/sqm (total maximum dose 360 mg/sqm) iv on day 56; MTX-IT - as in Induction on day 84/0 (omit oral MTX on day of MTX-IT).

Arm II: POMP (days 84/0 through 4): VCR - 1.5 mg/sqm iv on day 84/0; PRED - 40 mg/sqm in 3 divided doses on days 84/0 through 4; MTX-IT - as in Induction on day 84/0; MTX - 10 mg/sqm po on days 84/0 through 4; 6-MP - 500 mg/sqm on days 84/0 through 4. COP (days 21 through 25): VCR - 1.5 mg/sqm iv on day 21; PRED - 40 mg/sqm in 3 divided doses po on days 21 through 25; CTX - 30 mg/kg (900 mg/sqm) iv over 1 to 2 hours on day 21. POCA (days 42 through 46): VCR - 1.5 mg/sqm iv on day 42; PRED - 40 mg/sqm in 3 divided doses po on days 42 through 46; ADR - 30 mg/sqm iv on day 42; ARA-C - 75 mg/sqm iv, im, or sc on days 42 through 45. Moderate Dose MTX (days 63 through 66): MTX - 690-mg/sqm iv (75 mg/sqm iv over first hour and 15 mg/sqm/hour iv drip infusion over 41 hours using iv infusion pump) on day 63; CF - 12 mg/sqm po or iv q 6 hours for 7 doses starting at completion of MTX infusion.

Addendum, July 1980. Patients in bone marrow relapse while on therapy go off study. Patients in bone marrow relapse while off therapy remain on study and are reinduced with Induction/Intensification/Maintenance arm originally received, cranial irradiation excepted.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-ASP - 10,000 IU vials; PRED - 5 mg tablets; VCR -1 and 5 mg vials; MTX - 2 cc vials and 2.5 mg tablets; 6-MP - 50 mg tablets; CTX - 100 and 500 mg vials and 25 and 50 mg tablets; ADR - 10 mg vials; ARA-C - 100 and 500 mg vials; CF - 3 mg ampules and 50 mg vials.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 00860279

6.0005 PHASE III VCR/L-ASP/PRED REINDUCTION & VCR/MTX/L-ASP MAINTENANCE FOR CHILDHOOD ACUTE LYMPHOCYTIC OR UNDIFFERENTIATED LEUKEMIA

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PROTOCOL NUMBER(S) CCG-171

OBJECTIVES:

I. Determine the remission reinduction rate of vincristine (VCR)/L-asparaginase (L-ASP)/Prednisone (PRED) for patients with acute lymphocytic or acute undifferentiated leukemia relapsing with M-3 bone marrow (with or without CNS relapse) who are not receiving pulse reinduction (CCG-162 Maintenance Arm C) at time of relapse.

II. Determine the effects of reinduction with escalating MTX/L-ASP for patients failing to obtain M-1 or M-2 bone marrow on above regimen, relapsing during above reinduction pulses, or failing initial induction on CCG-161, 162, or 163.

III. Determine the length of Maintenance remission with escalating MTX/L-ASP (Capizzi regimen) for previously intensively treated children.

IV. Determine the effect of addition of VCR to maintenance with escalating MTX/L-ASP.

V. Determine the efficacy of Maintenance with systemic MTX to prevent CNS leukemic relapse.

PROTOCOL ENTRY CRITERIA: Children with acute lymphocytic or undifferentiated leukemia in M-3 bone marrow (or bone marrow plus other sites) relapse while on therapy in CCG-161, 162, 163, 141, 141A, 101, 143, or 905. Patients must not have had pancreatitis as a result of L-ASP therapy or severe hepatic or CNS toxicity from MTX. (Patients with an HLA, MLC matched sibling and are considering treatment by bone marrow transplant are eligible if they meet other criteria. Addendum 2, March 1980.)

PROTOCOL OUTLINE: Randomized study for Maintenance only. Enter all patients to re-induction Regimen A except those relapsing from CCG-162 maintenance or failing Induction on CCG-161, 162, or 163. Enter patients who do not qualify for Regimen A to Regimen B.

Reinduction:

Regimen A: 2-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; L-Asparaginase, L-ASP, NSC-109229; plus Prednisone, PRED, NSC-10023. For CNS relapse/prophylaxis (prophylaxis added in Addendum 1, November 1979): Intrathecal Therapy plus Radiotherapy. Methotrexate, MTX, NSC-740; plus Radiotherapy for nonresponders followed by Cytosine Arabinoside, ARA-C, NSC-63878; plus Hydrocortisone, HC, NSC-10483; for Maintenance.

Regimen B: 2-Drug Combination Chemotherapy. MTX, L-ASP.

For CNS relapse: Intrathecal Therapy plus Radiotherapy. As for Regimen A, but different schedule.

Maintenance: Randomize patients from Regimens A and B who have M-1 bone marrow to Arm I, II and III. (Patients with HLA, MLC matched sibling donor may elect bone marrow transplant upon achieving remission. Addendum 2, March 1980.)

Arm I: 2-Drug Combination Chemotherapy. MTX; L-ASP.

Arm II: 3-Drug Sequential Chemotherapy. VCR; MTX; L-ASP.

Arm III: 3-Drug Combination Chemotherapy. VCR; MTX; L-ASP.

Arm IV: Bone Marrow Transplant. Addendum 2, March 1980.

STRATIFICATION: Participating institutions; reinduction: Regimen A vs. Regimen B.

SPECIAL STUDY PARAMETERS: T and B cell markers, urine glucose, serum and CSF MTX levels, amylase, CSF studies (sugar, protein, cell count and culture), fibrinogen.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 120 to 125 patients will be entered.

DOSAGE SCHEDULE:

Reinduction:

Regimen A: VCR - 1.5 mg/sqm (maximum single dose 2 mg.) iv on days 1, 8, 15, and 22; L-ASP - 6000 IU/sqm im 3 times/week for a total of 9 doses starting on day 3; PRED - 40 mg/sqm po on days 1 through 28, then taper over 7 days. On day 29, randomize patients with M-1 bone marrow to maintenance and enter patients with M-2 or M-3 marrow to Regimen B for 4 courses. Randomize these patients to maintenance when they achieve M-1 marrow. Continue therapy for patients with M-2 marrow until they achieve M-1 or M-3 marrow, and remove patients with M-3 marrow from study to alternate therapy.

CNS Therapy: For patients with central nervous system relapse concomitant with initial bone marrow relapse: MTX - 6 mg (under 1 year), 8 mg (over 1 year up to 2 years), 10 mg (over 2 years up to 3 years), 12 mg (over 3 years) it 2 times/week for 6 doses. Give patients who fail to clear CSF after 6 doses 1200 rads craniospinal irradiation with whole brain boost to 1800 rads. If radiotherapy clears CSF give intrathecal maintenance therapy: ARA-C - 30 mg/sqm it (maximum 30 mg); HC - 15 mg/sqm it (maximum 15 mg), both q 2 months. Treat patients who fail to clear CSF at your discretion.

Regimen B: MTX - 100 mg/sqm (escalated by 50 mg/sqm/dose to toxicity) iv on day 1, then q 9 to 11 days; L-ASP - 15,000 IU/sqm im on day 2, then 24 hours after each MTX dose, both q 29 days for 4 courses. Randomize patients with M-1 bone marrow to maintenance, continue therapy for patients with M-2 marrow until they achieve M-1 or M-3 marrow, remove patients with M-3 marrow from study to alternate therapy.

CNS Therapy: For patients with central nervous system relapse during remission or for patients initially treated on Regimen B: MTX - dose as in Regimen A it on days 1, 5, and 10, and then q time MTX - iv is administered for a total of 6 doses; irradiation as in Regimen A. If CSF is cleared, give ARA-C, HC, MTX - doses as in Regimen A it q 2 months during maintenance.

Addendum 1, November 1979: For those patients who never have had CNS prophylaxis or relapse and undergo successful reinduction on either Regimen A or B, CNS prophylaxis should be administered at the initiation of maintenance therapy. Patients should receive MTX it on days 1, 5, 10, and thereafter on the day iv MTX is administered to a total of six doses, dosage as in Regimen A, CNS Therapy. In addition, whole brain irradiation to 1800 rads at 150 rads/fraction will be administered.

Maintenance:

Arm I: MTX - 100 mg/sqm (escalated 50 mg/sqm/dose to toxicity) iv on day 1, then q 9 to 11 days; L-ASP - 15,000 IU/sqm im on day 2, then 24 hours after each MTX dose.

Arm II: VCR - 1.5 mg/sqm (maximum 2 mg) iv on day 1, then q 9 to 11 days; MTX - as in Arm I iv on day 2, repeated 24 hours after each VCR dose. L-ASP as in Arm I on day 3.

Arm III: VCR; MTX, as in Arm II, given together on day 1; L-ASP as in Arm I given on day 2.

Arm IV: Bone marrow transplant, Addendum 2, March 1980.

Remove from study patients with M-3 bone marrow and enter to alternate therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; L-ASP - 10,000 IU vials; MTX - 50 mg vials; ARA-C - 100 and 500 mg vials; HC - 100 mg vials.

DATE SUMMARIZED: 04/80

6.0006 REINDUCTION OF REMISSION FOLLOWING FIRST BONE MARROW RELAPSE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) CCG-181

OBJECTIVES:

I. Reinduce remission in children with acute lymphoblastic leukemia who experience their first bone relapse while on chemotherapy by using 'standard' vincristine/prednisone/L-asparaginase chemotherapy.

II. Randomly compare intensive Maintenance chemotherapy with and without low-dose total body irradiation.

III. Evaluate the role of intensive chemotherapy/total body irradiation/allogeneic marrow transplantation vs. intensive Maintenance chemotherapy without marrow transplantation.

IV. Evaluate the role of relapse patterns (marrow alone vs. marrow plus other sites) on long-term survival.

V. Evaluate the role of cellular phenotypes (morphologic and immunologic) as prognostic factors in relapsed patients.

PROTOCOL ENTRY CRITERIA: Children with acute lymphoblastic leukemia who have experienced their first bone marrow relapse while on chemotherapy. Patients may have CNS or extramedullary relapse provided that it has occurred for the first time in that particular site. Marrow must be classed as M3. There must have been fewer than two previous courses of cranial or craniospinal radiotherapeutic courses prior to entry. Life expectancy must be at least 4 weeks.

PROTOCOL OUTLINE: Randomized study. Enter all patients on Regimen A. Among those patients who achieve M1 marrow status on days 28 or 42, assign those with a suitable marrow donor to Arm I and randomize the others to Arms II and III.

Regimen A: Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; L-asparaginase, L-ASP, NSC-109229; Methotrexate, MTX, NSC-740.

Intensification.

Arm I: 2-Drug Combination Chemotherapy plus Radiotherapy plus Immunotherapy. Cyclophosphamide, CTX, NSC-26271; MTX; plus total body irradiation (TBI) with supervoltage radiotherapy equipment; plus allogeneic bone marrow cells.

Arm II: 5-Drug Combination Chemotherapy plus Hormone Therapy. Cyclocytidine, CYC, NSC-145668; L-ASP; Adriamycin, ADR, NSC-123127; MTX; VCR; plus PRED.

Arm III: 5-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. CYC; L-ASP; ADR; MTX; VCR; plus PRED; plus TBI with supervoltage radiotherapy equipment.

STRATIFICATION BY: CNS involvement at time of relapse (yes vs. no), participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, bone marrow examination, liver and kidney function tests, lumbar puncture, immunologic markers, HLA typing, chest x-ray.

END POINTS: Response/remission rate, duration of response, survival.

CURRENT STATUS: About 234 patients are expected to accrue in 2 years.

DOSAGE SCHEDULE:

Regimen A: PRED - 40 mg/sqm/day po in 3 divided doses on days 0 through 28; VCR - 1.5 mg/sqm (maximum 2.0 mg) iv on days 0, 7, 14, 21, and 28; L-ASP - 6000 U/sqm im 3 times weekly beginning on day 4 for a total of 9 doses; MTX - 6-12 mg (depending on age) it on day 0 and day 14 in the absence of CNS disease, and weekly for 6 weeks in the presence of CNS disease. On day 28, patients with M1 marrows proceed to Arms I-III depending on availability of matched donor. Patients with M2 marrows receive additional VCR doses on days 35 and 42 and continue on PRED until day 42; those with M3 marrows go off study. On day 42, those with M1 marrows proceed to Arms I-III and those with M2 marrows are given another course of Induction.

Arm I: CTX - 60 mg/kg on days -5 and -4; MTX - 15 mg/sqm on days 1, 3, 6, 11, and 18 and 10 mg/sqm q week thereafter until day 100; TBI - 1000 rads at a slow dose rate on day -1; plus allogeneic bone marrow cells - 3-5 x 10 to the eighth nucleated marrow cells/kg on day 0.

Arm II: CYC - 600 mg/sqm sc on days 0, 1, 2, and 28; L-ASP - 500 U/kg im on day 5; ADR - 30 mg/sqm (total lifetime dose not to exceed 550 mg/sqm) iv on day 4; MTX - 100 mg/sqm iv (escalating by 50 mg/sqm until highest tolerated dose is reached) on days 0, 4, and 18; VCR - 1.5 mg/sqm iv on day 21; plus PRED - 40 mg/sqm po on days 21 through 25.

Arm III: CYC - 600 mg/sqm sc on days 2, 3, 4, 28, 29, and 30; L-ASP - 500 U/kg im on days 7 and 33; ADR - 30 mg/sqm iv (total lifetime dose not to exceed 550 mg/sqm) on days 6 and 32; MTX - 100 mg/sqm iv on days 2, 6, 28, and 32, escalating by 50 mg/sqm until highest tolerated dose is reached; VCR - 1.5 mg/sqm iv on days 21 and 49; and PRED - 40 mg/sqm po on days 21 through 25 and 49 through 53; plus TBI - 50 rads on days 0 and 56.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; PRED - 5 mg tablets; L-ASP - 10,000 IU vials; MTX - 5 and 50 mg vials; CTX - 100 and 500 mg vials and 25 and 50 mg tablets; ADR - 10 mg vials; CYC - 100 and 500 mg vials.

DATE SUMMARIZED: 12/80

6.0007 TOTAL SANCTUARY VS CONVENTIONAL CNS TREATMENT FOR NEWLY DIAGNOSED ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) CCG-191P; NCI-POB-7702

OBJECTIVES:

I. Compare the effects of high-dose, protracted intravenous methotrexate infusions with intrathecal methotrexate plus standard cranial irradiation on: central nervous system relapse; central nervous system toxicity, acute and delayed; hematologic remission induction and duration; non-CNS extramedullary relapse (e.g., testes); and survival.

PROTOCOL ENTRY CRITERIA: Previously untreated patients less than 21 years of age with acute lymphoblastic leukemia who are less than 3 years old or are 7 years of age or older, or who have an initial WBC greater than 10,000/cumm. Patients with acute undifferentiated leukemia of any initial WBC or age are eligible. Patients may not have Burkitt's cell leukemia or meningeal leukemia.

PROTOCOL OUTLINE: Randomized study.

Arm I:

Induction: 5-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; L-Asparaginase, L-ASP, NSC-109229; Daunomycin, DNM, NSC-82151; Allopurinol, NSC-1390; Methotrexate, MTX, NSC-740; plus Prednisone, PRED, NSC-10023.

Consolidation: 3-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. VCR; 6-Mercaptopurine, 6-MP, NSC-755; MTX; plus PRED; plus cranial supervoltage irradiation (Co-60, 4 and 6 MeV Linacs, or higher photon energies, not to exceed 10 MeV).

Maintenance: Multiple-Drug Cyclical-Sequential Chemotherapy plus Hormone Therapy. POMP: VCR; MTX; 6-MP; PRED; followed by VAP: VCR; L-ASP; PRED; followed by VDP: VCR; DNM; PRED; followed by 6-MP; MTX; Cyclophosphamide, CTX, NSC-26271.

Arm II:

Induction: 6-Drug Combination Chemotherapy plus Hormone Therapy. VCR; L-ASP; DNM; Allopurinol; MTX; Citrovorum Factor, CF, NSC-3590; plus PRED.

Consolidation: 3-Drug Combination Chemotherapy plus Hormone Therapy. VCR; 6-MP; MTX; plus PRED.

Maintenance: Multiple-Drug Cyclical-Sequential Chemotherapy plus Hormone Therapy. POMP-24; VAP; VDP; 6-MP; MTX; CTX.

STRATIFICATION BY: Participating institutions; age: 2 to 10 years old vs. less than 2 and more than 10 years old; blood counts: WBC greater than 25,000/cumm vs. WBC less than 25,000/cumm.

SPECIAL STUDY PARAMETERS: Psychological evaluation, CT brain scan, lumbar puncture, CSF for methotrexate levels and for storage.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, recurrence rate.

CURRENT STATUS: 162 patients will be entered.

DOSAGE SCHEDULE:

Arm I:

Induction:

VCR - 1.5 mg/sqm iv on days 1, 8, 15, and 22 (single dose not to exceed 2 mg); L-ASP - 6000 I.U./sqm im starting on day 5 then q M, W, and F for a total of 9 doses; PRED - 40 mg/sqm po in 3 divided doses on days 1 through 28; DNM - 30 mg/sqm iv on days 1, 8, and 15; MTX - 6 to 12 mg it (dosage age-dependent) on day 2; Allopurinol - 100 mg/sqm iv or po tid until circulating blast cell count is less than 1000/cumm. Induction phase will be 28 days in length. Rest for 7-10 days before Consolidation.

Consolidation:

VCR - 1.5 mg/sqm iv on days 1, 15, and 29 (maximum single dose 2 mg); PRED - 40 mg/sqm po on days 1 through 7, 15 through 21, and 29 through 35; 6-MP - 75 mg/sqm po on days 1 through 35; cranial irradiation - 1800 to 2400 rads (dose age-dependent) given at 200 rads/day on days 3 through 5, 8 through 12, and 15 through 18; MTX - 6 to 12 mg it on days 1, 8, 15, and 22. Consolidation phase will be 35 days in length. Rest for 7-10 days before Maintenance.

Maintenance:

Six cycles of 22 weeks each. Week 1: POMP: PRED - 40 mg/sqm po on days 1 through 5; VCR - 1.5 mg/sqm iv on day 1 (maximum single dose 2 mg); MTX - 7.5 mg/sqm po on days 1 through 5; 6-MP - 500 mg/sqm po on days 1 through 5 (without Allopurinol). Week 2: rest period. Weeks 3 through 6: 6-MP - 75 mg/sqm po daily; MTX - 7.5 mg/sqm po twice weekly, e.g., T and F. Weeks 7 and 8: VAP: VCR - 1.5 mg/sqm iv on days 1 and 8; L-ASP - 6,000 I.U./sqm im on days 1, 3, 5, 8, 10, and 12; PRED - 40 mg/sqm po in 3 divided doses on days 1 through 14. Week 9: CTX - 5 mg/kg po on days 1 through 5. Weeks 10 through 13: 6-MP - 5 mg/sqm po daily; MTX - 7.5 mg/sqm po twice weekly. Weeks 14 and 15: VDP: VCR - 1.5 mg/sqm iv on days 1 and 8; DNM - 20 mg/sqm iv on days 1 and 8; PRED - 40 mg/sqm po in 3 divided doses on days 1 through 14. Week 16: rest period. Weeks 17 through 20: 6-MP - 75 mg/sqm daily; MTX - 7.5 mg/sqm po twice weekly. Week 21: CTX - 5 mg/kg po on days 1 through 5. Week 22: rest period. Week 23: Begin repeat course for a total of 6 entire cycles, after which all Chemotherapy ceases.

Arm II:

Induction:

VCR, L-ASP, PRED, DNM, and Allopurinol given as in Arm I. MTX - 6000 mg/sqm priming dose iv over first hour, an infusion of 1200 mg/sqm/hour over the succeeding 23 hours (total dose including priming dose is 33,600 mg/sqm). 12 hours following completion of MTX infusion, CF is given iv initial dose of 200 mg/sqm over 1 hour, then 3 hours later, and every 3 hours for 5 additional doses, in a dose of 12 mg/sqm iv or po, then every 6 hours, 12 mg/sqm iv or po until MTX level is equal to or less than 8 x 10 to the eighth M. Induction phase is 28 days. Rest 7 to 10 days.

Consolidation:

VCR, PRED, and 6-MP given as in Arm I. MTX - 1200 mg/sqm/hour iv infusion on days 1, 15, and 29. Consolidation phase is 35 days. Rest for 7-10 days.

Maintenance:

6 cycles of 22 weeks each. Week 1: POMP-24: PRED, VCR, and 6-MP given as in Arm I. MTX - 6000 mg/sqm priming dose iv infusion given over first hour, 1200 mg/sqm/hour over next 23 hours. 12 hours following completion of MTX infusion CF is given iv initial dose of 200 mg/sqm over 1 hour, then 3 hours later and every 3 hours for 5 additional doses, 12 mg/sqm iv or po, then every 6 hours at same dosage until MTX level is equal to or less than 8 x 10 to the eighth M. Week 2: rest period. Weeks 3, 4, 5, and 6: 6-MP and MTX given as in Arm I. Weeks 7 and 8: VAP: VCR, L-ASP, and PRED given as in Arm I. Weeks 9 and 10 through 13: CTX, 6-MP, and MTX given as in Arm I. Weeks 14 through 22: VDP: VCR, DNM, PRED, 6-MP, MTX, and CTX given as in Arm I. Week 23: Begin repeat course for a total of 6 entire cycles, after which all Chemotherapy ceases.

The following conditions will result in removal from protocol treatment: M3 bone marrow after completing 28 days of Induction therapy (suspicious M2 bone marrows should be repeated at 2-week intervals until M1 or M3); extramedullary leukemia, i.e., CNS, testes, ovary, skin, etc., demonstrated by aspirate or biopsy specimen.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-ASP - 10,000 I.U. vials; PRED - 5 mg tablets; VCR - 1 and 5 mg vials; MTX - 1 g vials (as revised by Addendum 1, June 1980); 6-MP - 50 mg tablets; CTX - 100 and 500 mg vials, 25 and 50 mg tablets; DNM and Allopurinol not given; CF - 50 mg vials (as revised by Addendum 1, June 1980).

DATE SUMMARIZED: 10/80

6.0008 EVALUATION OF MAINTENANCE THERAPY AFTER LONG-TERM CHEMOTHERAPY FOR CHILDREN IN REMISSION FROM ACUTE LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) CCG-905

OBJECTIVES:

I. Determine the role of chemotherapy in maintenance of prolonged initial remission.

II. Obtain data on the pattern of relapse during prolonged remission comparing continuous chemotherapy with interruption of therapy.

III. Determine whether prolonged chemotherapy with antineoplastic and immuno-suppressive agents predisposes a patient to eventual relapse by suppression of host immune response.

PROTOCOL ENTRY CRITERIA: Children with acute leukemia in initial remission of disease for 3 or more years following continuous chemotherapy. Patients must be in disease status 4 and many have been previously treated on protocols CCA-401, L-7 Study, CCA-601, Plasma Adjuvant Study, CCG-803 or CCG-903. Patients from Regimens 2, 4 or 5 who exit from Regimen 6 in CCG-903 because of toxicity may be entered to non-randomized part of this study.

PROTOCOL OUTLINE: Randomized or paired study.

Enter initial group of patients in matched pairs according to specified disease parameters and therapy. Randomize subsequent patients in blocks of two. Separately randomize patients from protocol CCG-803.

Arm I: Maintenance Chemotherapy. Continue current chemotherapy.

Arm II: Control. Discontinue current chemotherapy.

Perform L.P.'s on all patients prior to study entry. Collect serum for immunoglobulin determinations. Repeat PPD skin test until negative on all patients in remission on BCG. Remove patients from study when disease status A changes to C or D, with M-3 bone marrow status.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Immunoglobulin determinations, PPD for patients on BCG.

END POINTS: Recurrence rate, duration of remission, survival rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE: Not applicable.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 09/76

PATIENT ACCRUAL: 01031078

6.0009 NO THERAPY VS SHORT-TERM CHEMOTHERAPY FOLLOWING TERMINATION OF MAINTENANCE FOR PEDIATRIC ALL AFTER 3-YEAR CONTINUOUS COMPLETE REMISSION

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PROTOCOL NUMBER(S) CLB-7611R

OBJECTIVES:

I. Determine whether late intensification with prednisone, vincristine, L-asparaginase, and it methotrexate can prevent relapse in acute lymphocytic leukemia patients who have been in continuous complete remission for 3 years. This is Addendum 1 to Protocol CLB-7611.

PROTOCOL ENTRY CRITERIA: All acute lymphocytic leukemia patients entered into Protocol CLB-7611 who have remained in continuous remission for at least 3 years. Patients with extramedullary relapses that have been controlled are eligible if they remain in continuous complete remission for 3 years after their localized disease has been eradicated.

PROTOCOL OUTLINE: Randomized study.

After an 8-week rest period following Maintenance Therapy on CLB-7611, stratify patients according to sanctuary therapy and sex, then randomize to Arm I or Arm II.

Arm I: No further therapy. Follow until relapse.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; L-Asparaginase, L-ASP, NSC-106977; Methotrexate, MTX, NSC-740; plus Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Participating institutions, sex, sanctuary therapy.

SPECIAL STUDY PARAMETERS: Hematologic parameters including bone marrow aspiration/biopsy, testicular biopsy, blood glucose, renal and hepatic function studies, CSF studies.

END POINTS: Disease-free interval, recurrence rate, survival rate, length of survival.

CURRENT STATUS: 150 patients will be randomized to each arm.

DOSAGE SCHEDULE:

Arm I: No therapy. Follow until relapse.

Arm II: VCR - 2 mg/sqm iv (maximum 2 mg) on days 1, 8, 15, and 22; L-ASP - 1000 units iv infusion over 30 minutes on days 29 through 38; MTX - 12 mg/sqm it (maximum 15 mg) on days 1, 8, 15, and 22; PRED - 40 mg/sqm po on days 1 through 28, then taper over 1 week.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PRED - 5 and 50 mg tablets; VCR - 1 and 10 mg ampules; L-ASP - 10,000 unit vials; MTX - 5 and 10 mg vials.

DATE SUMMARIZED: 07/80

6.0010 PHASE III MTX/PRED/VCR INDUCTION, CNS PROPHYLAXIS, CHOP AND 6-MP/MTX/VCR/PRED WITH OR WITHOUT ARA-C/CTX/MEPRDL/ADR FOR ALL

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PROTOCOL NUMBER(S) SEG-78ALL333

OBJECTIVES:

I. Reaffirm the efficacy of induction chemotherapy with vincristine (VCR), methotrexate (MTX) and high-dose prednisone (PRED) hormone therapy for acute lymphoid leukemia.

II. Consolidate remissions using moderately intensive chemotherapy with CHOP: cyclophosphamide (CTX)/adriamycin (ADR)/VCR/PRED, plus CNS prophylaxis by irradiation and intrathecal (IT) MTX.

III. Compare efficacy of maintenance with 6-Mercaptopurine (6-MP), MTX, PRED and VCR pulses versus the same regime plus late intensification therapy with Cytosine arabinoside (ARA-C), CTX, ADR, and high-dose methyl Prednisolone (MEPRDL) for maintaining complete remissions.

IV. Assess terminal deoxynucleotidyl transferase, glucocorticoid receptors and immunologic membrane markers as prognostic factors.

PROTOCOL ENTRY CRITERIA: Patients over 15 years old with acute lymphoblastic, prolymphocytic, lymphosarcoma or lymphoma leukemia. Patients must be without CNS disease and must not have had prior therapy except less than seven days' treatment with corticosteroids. They must have adequate cardiac and renal function.

PROTOCOL OUTLINE: Randomized study for Maintenance only.

Induction:

2-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67474; Methotrexate, MTX, NSC-740; plus Prednisone, PRED, NSC-10023.

Consolidation:

Regimen A: 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; VCR, plus PRED.

CNS Prophylaxis: Cranial Radiotherapy, Intrathecal and 2-Drug Combination Chemotherapy.

Regimen B: CHOP plus MTX (IT).

Maintenance: Randomize complete responders (CR) to Arm I or Arm II.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy plus (IT) Chemotherapy. 6-Mercaptopurine, 6-MP, NSC-755; MTX; VCR; plus PRED followed by MTX (IT).

Arm II: Maintenance as in Arm I, plus late Intensification. 4-Drug Combination Chemotherapy plus Hormone Therapy. 6-MP; MTX; VCR; PRED; MTX (IT); followed by Cytosine arabinoside, ARA-C, NSC-63878; ADR; CTX; and Methyl Prednisolone, MEPRDL, NSC-19987.

STRATIFICATION BY: For Maintenance arms only: terminal transferase: positive vs. negative; immunologic cell type: null vs. T vs. B cell vs. technically inadequate.

SPECIAL STUDY PARAMETERS: Membrane marker studies for T and B cells, terminal transferase assay, bone marrow biopsy, glucocorticoid receptors, karyotype analysis.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, duration of remission, survival.

CURRENT STATUS: At least 113 patients will be entered.

DOSAGE SCHEDULE:

Induction:

Give a maximum of two 21-day courses. MTX - 8 mg/sqm po in 4 divided doses on days 1, 5, 8, 12, 15, 19; PRED - 350 mg/sqm po on days 1 through 10, then 50 mg/sqm po q other day. Enter complete responders (CR) after one course to consolidation. Remove from study partial responders (PR) or nonresponders (NR) after 2nd course.

Consolidation:

Repeat course after 21 days for a total of 2 courses.

Regimen A: CHOP. CTX - 750 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; VCR - 1 mg/sqm (maximum 2 mg) iv on day 1; PRED - 50 mg/sqm po on days 1 through 5. At the end of 2 courses proceed to CNS Prophylaxis. Remove patients with CNS leukemia from study.

CNS Prophylaxis: 2.5 week course. MTX - 12 mg/(IT) twice a week for 3 weeks plus cranial radiation - 2400 rad over 2 1/2 weeks. Give PRED and VCR during CNS treatment, as in Regimen A. Enter patients to Regimen B three weeks after beginning CNS Prophylaxis.

Regimen B: Repeat course q 21 days for a total of 4 courses. CHOP - same dosage as in Regimen A followed by MTX - 12 mg/(IT) on day 1 of first and last course. Randomize CR to Maintenance after a total of six Consolidation courses. Remove from study patients who develop CNS leukemia.

Maintenance: Repeat course q 8 weeks for a total of 72 weeks.

Arm I: 6-MP - 50 mg/sqm/day po; MTX - 20 mg/sqm po or iv q 7 days; PRED - 50 mg/sqm po on days 1 through 14 q 8 weeks; VCR - 1 mg/sqm (maximum 2 mg) iv on days 1, 8, and 15 q 8 weeks; MTX - 12 mg it on day 1 q 8 weeks. Evaluate patients. If CR is maintained, stop all therapy.

Arm II: 6-MP, MTX, PRED, VCR, MTX-IT, as in Arm I, followed by late Intensification every 24 weeks. ARA-C - 100 mg/sqm iv continuous infusion on days 1 through 5; ADR - 50 mg/sqm iv on day 1; CTX - 500 mg/sqm iv on day 1; MEPRDL - 280 mg/sqm iv on days 1 through 5. Resume standard maintenance therapy 4 weeks after beginning late Intensification. Remove from study patients with proven CNS leukemia.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 5 & 50 mg vials; VCR - 1 & 5 mg ampules; PRED - 5, 20, & 50 mg tablets; CTX - 100, 200, & 500 mg vials; ADR - 10 & 50 mg vials; ARA-C - 100 mg vials; 6-MP - 50 mg tablets; MEPRDL - 40, 125, 500, & 1000 mg vials.

DATE SUMMARIZED: 06/79

6.0011 PHASE III CHEMOTHERAPY WITH INTRAVENOUS VS INTRAMUSCULAR L-ASP PLUS VCR/PRED FOR ACUTE LYMPHOCYTIC LEUKEMIA IN CHILDREN

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PROTOCOL NUMBER(S) SWOG-7606

OBJECTIVES:

I. Investigate whether the intramuscular route of administration of L-asparaginase (L-ASP), in combination with vincristine (VCR) and prednisone (PRED), is less toxic than the intravenous route in remission Induction of children with acute lymphocytic leukemia.

II. Evaluate the clinical effectiveness of intravenous versus intramuscular L-ASP in combination with VCR and PRED in the induction of remission in children with acute lymphocytic leukemia.

PROTOCOL ENTRY CRITERIA: Patients under 18 years of age with acute lymphocytic leukemia, acute undifferentiated leukemia or acute stem cell leukemia not eligible for protocols of higher priority.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; L-Asparaginase, L-ASP, NSC-109229, given iv.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. VCR, PRED and L-ASP given im.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Fasting blood sugar; CSF studies; liver, spleen and lymphnode measurements.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, remission duration.

CURRENT STATUS: 150 patients will be entered in one year.

DOSAGE SCHEDULE:

Arm I: VCR - 2.0 mg/sqm (maximum dose 2 mg) iv on days 0, 7, 14 and 21; PRED - 60 mg/sqm/day in 3 to 4 divided doses for 28 days, then taper to discontinue over a period of 7 days; L-ASP - 1000 I.U./sqm/day iv for 14 days.

Arm II: VCR, PRED as in Arm I; L-ASP - 1000 I.U./sqm/day im for 14 days.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-ASP - 10,000 I.U. vials; VCR - 1 and 5 mg vials; PRED - 5 mg tablets.

DATE SUMMARIZED: 02/77

6.0012 RADIOTHERAPY, CHEMOTHERAPY WITH VCR/PRED/L-ASP/MTX/6-MP, CTX, ARA-C, DNM & HYDROCORTISONE FOR ACUTE CHILDHOOD LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-7623; MDAR-197; SWOG-ALINC-12

OBJECTIVES:

I. Evaluate the necessity for treatment with maximum tolerated, therapeutic dose levels with moderate to severe myelosuppression as compared to moderate dose levels with minimal to mild myelosuppression by using survival and duration of remission as an index of response.

II. Compare two treatment regimens, patterned after the regimens currently in use in the previous study (Alinc #11) for children with poor-prognosis leukemia in order to isolate the subset of poor prognosis of the pediatric patient population.

III. Evaluate the feasibility of prospectively identifying patients with T- and B-cell leukemia to facilitate treatment with the appropriate protocol.

IV. Examine the question of pulse intensification during therapy by comparing the remission duration of patients in this study (Alinc #12) with the ongoing development of the outcome of the previous study (Alinc #11).

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age who have been diagnosed with acute lymphoblastic leukemia (ALL), acute undifferentiated leukemia (AUL) or acute stem cell leukemia (ASL). Exclude other forms of leukemia which do not obviously fall into these categories. Specify good or poor prognosis category and either presence or absence of T-cell markers and also, if possible, evaluate B-cell markers.

PROTOCOL OUTLINE: Randomized study.

Regimen A: Enter patients 1-2 years of age with wbc count of less than 10,000 cumm, 3-5 years of age with wbc count below 10,000 or up to 99,999, and 6-10 years of age with wbc of less than 10,000, cumulative absence of all surface markers and without hepatography, splenomegaly or extramedullary disease or mediastinal mass.

Arm I: 4-Drug Combination Chemotherapy and Hormone Therapy plus Cranial Radiotherapy. Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; L-Asparaginase, L-ASP, NSC-109229; Methotrexate, MTX, NSC-740; 6-Mercaptopurine, 6-MP, NSC-755.

Arm II: 4-Drug Combination Chemotherapy and Hormone Therapy. VCR; PRED; L-ASP; MTX; 6-MP, with periods of omission of PRED.

Regimen B: Enter all patients below 1 year of age, 1-2 years of age with wbc count from 10,000 to 100,000 cumm, 3-5 years of age with wbc count at or above 100,000 cumm, 6-10 years of age with wbc count of 10,000 to above 100,000 cumm, over 10 years of age with wbc count from below 10,000 to at or above 100,000 cumm, or patients with any massive extramedullary disease.

Arm III: 4-Drug Combination Chemotherapy and Hormone Therapy. VCR; PRED; L-ASP; MTX; 6-MP.

Arm IV: Induction: 6-Drug Combination Chemotherapy and Hormone Therapy plus Radiotherapy. VCR; PRED; L-ASP; Cyclophosphamide, CTX, NSC-26271; MTX; Hydrocortisone, HC, NSC-10483; Cytosine arabinoside, ARA-C, NSC-63878; 6-MP.

Regimen C: Enter patients with T- or B-cell markers present.

Arm V: Same as Protocol 7615 SLA2L2. 4-Drug Combination Chemotherapy and Hormone Therapy plus Radiotherapy. CTX; VCR; PRED; MTX; Daunomycin, DNM, NSC-82151.

STRATIFICATION BY: Good prognosis or poor prognosis on the basis of age, wbc, B- and T-cell markers on lymphoblasts, absence of significant hepatomegaly or extramedullary disease.

SPECIAL STUDY PARAMETERS: BUN, creatinine, uric acid, alkaline phosphatase, SGOT/SGPT, serum lipase, amylase, fasting blood sugar, fibrinogen, bone marrow CSF studies, and at time of diagnosis, IVP and skeletal survey.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response.

CURRENT STATUS: 253 patients will be entered: 108 with good prognosis and 145 with poor prognosis.

DOSAGE SCHEDULE:

Regimen A: Induction: Administer VCR and PRED for either 4 or 6 weeks to obtain M1 marrow status. Discontinue treatment if M1 marrow status is not achieved. Randomize to:

Arm I: VCR - 1.5 mg/sqm/week iv x 4 weeks (maximum 2.0 mg). PRED - 40 mg/sqm/day po in 3 or 4 divided daily doses tapered during 1 week. L-ASP - 10,000 units/sqm/week iv x 2 weeks. CNS therapy beginning week 5. MTX - 12 mg/sqm twice q week intrathecally for 5-7 weeks. Cranial Radiotherapy Cobalt 60 or 4-6 MeV Linac Supervoltage - 2250-2500 total dose divided into 5 fractions per week given for 2 1/2 weeks together with MTX IT. Reduce dose to 2000 rads for children of 1-2 years of age and 1500 rads for infants less than 12 months of age.

Maintenance therapy beginning at remission. All patients receive 6-MP - 50 mg/sqm/day po and MTX - 20 mg/sqm po q week beginning week 8 except when IT therapy is given. Reinforcement therapy q 4 months at weeks 20, 36, 53, etc. VCR and PRED as in Induction therapy. Patients are randomized for wbc maintenance; the wbc count is maintained at 3000-4500/cumm or at 1500-3000/cumm by adjusting the PRED dosage.

Arm II: Same as Arm I but wbc count is maintained at 3000-4500/cumm by interrupting treatment with PRED.

Regimen B: Induction: Administer VCR and PRED for either 4 or 6 weeks to obtain M1 marrow status. Discontinue treatment if M1 marrow status is not achieved. Randomize to:

Arm III: VCR; PRED; L-ASP; MTX; 6-MP as in Arm I.

Arm IV: VCR - 2.0 mg/sqm/week iv for 4 or 6 weeks (maximum 2 mg/week); PRED - 60 mg/sqm/day po in 3 or 4 divided doses for 4 weeks (minimum 20 mg/day, maximum 60 mg/day) tapered over 1 week. Consolidation: L-ASP - 6000 units/sqm/day on days 29 through 42; CTX - 1000 mg/sqm iv on days 30 and 43. Triple intrathecal therapy beginning on day 57 q 6 weeks for 6 courses; MTX - 15 mg/sqm it (maximum dose 15 mg) on days 58 through 61; HC - 15 mg/sqm it (maximum dose 15 mg); ARA-C - 30 mg/sqm it (maximum dose 30 mg) given singly in above sequence. MTX - 15 mg/sqm/day for 4 days on day following triple intrathecal therapy q 2 weeks for 6 courses. Maintenance: 6-MP - 50 mg/sqm/day, beginning week 21; MTX - 20 mg/sqm/week po when it MTX is not given, beginning week 21.

Regimen C: Induction: CTX - 120 mg/sqm iv on day 1; VCR - 2.0 mg/sqm (maximum 2.0 mg) iv q week on day 3 or 4 for 4 weeks; PRED - 60 mg/sqm/day po divided into 4 doses for 4 weeks; with tapering during last week. Radiotherapy - 3000 rads total dose during 4 weeks depending upon extra-abdominal primary. MTX - 6.25 mg/sqm IT, once between 1st and 2nd VCR injection and twice again, 3 days apart during decremental PRED; DNM - 60 mg/sqm iv on 2 successive days between 2nd and 3rd VCR injection. MTX - 6.25 mg/sqm twice, 3 days apart during decremental PRED.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PRED - 5 mg tablets; HC - 100 mg vials; VCR - 1 and 5 mg vials; MTX - 2.5 mg tablets; L-ASP - 10,000 IU vials; 6-MP - 50 mg tablets; CTX - 100, 200 and 500 mg vials; ARA-C - 100 mg vials.

DATE SUMMARIZED: 01/77

PATIENT ACCRUAL: 04450279

6.0013 PHASE III INTRATHECAL MTX/ARA-C/HC/CF PLUS INDUCTION AND RADIOTHERAPY FOR FIRST CNS RELAPSE IN ACUTE LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-7712; MDAR-277; SWOG-CNS Leuk. Study 6

OBJECTIVES:

I. Compare two therapies for CNS leukemia with respect to length of CNS remission and CNS toxicity: CNS remission induction with intrathecal (IT) methotrexate (MTX)/hydrocortisone (HC)/cytosine arabinoside (ARA-C), and im or iv citrovorum factor (CF), followed by cranial irradiation and intrathecal MTX vs. CNS remission induction with above IT therapy followed by craniospinal irradiation.

II. Compare two therapies for CNS leukemia with respect to bone marrow toxicity, length of subsequent bone marrow remission and survival.

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age at the time of their initial diagnosis with a first CNS relapse of acute lymphocytic leukemia. Patients must not have had more than one marrow relapse, prior spinal irradiation, cranial irradiation with more than 2500 rads, nor prior severe toxicity in response to intrathecal MTX or ARA-C.

PROTOCOL OUTLINE: Randomized study. Patients are randomized to Arms I and II for Maintenance at diagnosis of CNS disease. Patients are initially treated on Induction regimen; they then proceed to the appropriate Maintenance arm.

Induction: 2-Drug Intrathecal Combination Chemotherapy plus Intrathecal Hormone Therapy plus CF Rescue. Methotrexate, MTX, NSC-740; Hydrocortisone, HC, NSC-10483; Cytosine arabinoside, ARA-C, NSC-63878; Citrovorum Factor, CF, NSC-3590.

Maintenance:

Arm I: Cranial Radiotherapy plus Intrathecal Therapy. MTX; HC; ARA-C; CF.

Arm II: Craniospinal Radiotherapy. Megavoltage equipment: Cobalt-60, 2 MeV x-rays or higher.

STRATIFICATION BY: Participating institutions, time of CNS relapse, bone marrow status, prior cranial radiotherapy.

SPECIAL STUDY PARAMETERS: Bone marrow aspirate, CSF examination, fundoscopy, testicular measurements.

END POINTS: Response/remission rate, duration of remission, relapse rate, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: 72 patients will be entered in 3.5 years.

DOSAGE SCHEDULE: Concurrent with CNS therapy, give all M1 patients systemic reinforcement therapy and M2 and M3 patients systemic Induction therapy according to SWOG priorities.

Induction: MTX - 15 mg/sqm (maximum dose 15 mg) it on day 1; HC - 30 mg/sqm it on day 1; ARA-C - 60 mg/sqm (maximum dose 60 mg) it on day 1; CF - 15 mg/sqm (maximum dose 15 mg) iv or im. Omit CF if systemic MTX is substituted for MTX-IT. Repeat q week for 6 courses, then remove from study patients not in remission.

CNS Maintenance:

Arm I: 2400 rads to the cranium in 2.5 weeks beginning 1 week after 6 courses of Induction. MTX, HC, ARA-C, and CF as in Induction, beginning 2 weeks after completion of cranial irradiation and given at increasing time intervals: 4, 6 then q 8 weeks, to be continued for at least 2 years unless there is bone marrow, extramedullary or CNS relapse.

Arm II: 2400 rads to the cranium in 2.5 weeks and 1400 rads concurrently to the spine, beginning 1 week after 6th course of Induction.

Follow all patients for life.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 500 mg vials; ARA-C - 100 mg vials; HC - 100 mg vials; CF - 3 mg vials; Elliott's B Solution - 10 ml ampules.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 00210179

6.0014 PHASE II CHEMOTHERAPY WITH ANGUIDINE FOR PEDIATRIC AND ADOLESCENT ACUTE LYMPHOBLASTIC LEUKEMIA IN RELAPSE

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PROTOCOL NUMBER(S) SWOG-7810

OBJECTIVES:

I. Determine the clinical efficacy of anguidine (ANG) as indicated by the induction of partial or complete remission in pediatric and adolescent patients with acute lymphoblastic leukemia in relapse.

II. Observe for factors predisposing to excessive myelosuppression and for other toxicities not observed during Phase I studies of this drug.

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age with lymphoid malignancy, disseminated in relapse, previously diagnosed as acute leukemia or lymphoma and who are either not eligible for protocols of higher priority or are resistant to standard forms of therapy. Patients must have an M3 marrow with greater than 25% blasts and must not have had prior therapy with anguidine.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Anguidine, ANG, NSC-141537.

STRATIFICATION BY: Participating institutions, number of prior relapses.

SPECIAL STUDY PARAMETERS: Tests of renal and hepatic function, fasting glucose levels, bone marrow analysis, lumbar puncture with cytology, in vitro tumor cell studies.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 40 to 50 patients will be entered in 2 to 2.5 years.

DOSAGE SCHEDULE:

ANG - 4.5 mg/sqm iv 4 hour infusion on days 1 through 5 q 4 weeks. After 4 weeks discontinue therapy for patients in remission with M3 marrow, or with unimproved M3 marrow. Continue therapy if patient is in partial remission as indicated by an M1 or M2 marrow.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ANG - 10 mg vials.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00310179

6.0015 PHASE III ARA-C/TG/COAP WITH VS WITHOUT VAP MAINTENANCE PLUS CNS THERAPY AFTER VAP REINDUCTION FOR FIRST-RELAPSE PEDIATRIC ALL

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PROTOCOL NUMBER(S) SWOG-7834; SWOG-SIMAL-2; MDAR-341

OBJECTIVES: (This protocol replaces SWOG-7721).

I. Determine in children in the first relapse of acute lymphoblastic leukemia (ALL) the remission duration which can be achieved following an intensive and aggressive Induction regimen of cyclic combination chemotherapy and hormone therapy with VAP: vincristine (VCR)/adriamycin (ADR)/prednisone (PRED) and Maintenance combination chemotherapy and hormone therapy with cytosine arabinoside (ARA-C), thioguanine (TG), COAP: cyclophosphamide (CTX), VCR, ARA-C, PRED plus VAP AND CNS prophylaxis with methotrexate (MTX), hydrocortisone (HC) and ARA-C.

II. Investigate the value of repeated intensive reinduction during remission maintenance on the duration of remission in patients with acute lymphocytic leukemia after the first relapse.

III. Evaluate and compare the toxicities of the therapeutic regimens employed on this protocol including the various radiotherapy regimens.

IV. Standardize primary relapse treatment schedules in patients with ALL at first relapse.

V. Further accrue data regarding prognostic factors for salvage in patients having a first relapse on standard therapy.

VI. Compare the results with those obtained with SWOG 7637 (SIMAL-1) as a historical control.

PROTOCOL ENTRY CRITERIA: Patients under age 21 in first relapse of ALL in bone marrow, CNS, or extramedullary (EMD), or any combination of these sites. Previously treated patients with CNS and/or EMD disease at initial diagnosis and patients maintained on 6-MP, alone or in combination, who are in first bone marrow relapse and patients who failed on SWOG-7623 are eligible. Patients may not have had prior therapy with ADR, daunomycin, TG or systemic ARA-C, and they may not have had a previously treated relapse. Patients in their first CNS relapse and patients with EMD disease must be concurrently registered on the CNS #6 SWOG-7712 or EMD protocol, respectively, if eligible.

PROTOCOL OUTLINE: Study randomized for Maintenance only.

Induction. Enter all patients to Regimen A; those who fail to respond go to Regimen B.

Regimen A: 2-Drug Combination Chemotherapy plus Hormone Therapy. VAP: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; and Prednisone, PRED, NSC-10023.

Regimen B: 2-Drug Combination Chemotherapy. TA: Thioguanine, TG, NSC-752; Cytosine arabinoside, ARA-C, NSC-63878.

Maintenance. Randomize all responders from Regimen A. Enter all patients from Regimen B to Arm I only.

Arm I: 2-Drug Combination Chemotherapy alternating with 3-Drug Combination Chemotherapy and Hormone Therapy, plus Intrathecal CNS Prophylaxis: 3-Drug Combination Chemotherapy plus Hormone Therapy. TA: TG; ARA-C; alternating with COAP: Cyclophosphamide, CTX, NSC-26271; VCR; ARA-C; PRED; plus intrathecal Methotrexate, MTX, NSC-740; ARA-C; Citrovorum factor, CF, NSC-3590; and Hydrocortisone, HC, NSC-10483.

Arm II: 2- and 3-Drug Alternating Combination Chemotherapies, plus reinforcement with 2-Drug Combination Chemotherapy plus Hormone Therapy plus Intrathecal CNS Prophylaxis. TG; ARA-C; alternating with COAP, as in Arm I; plus VAP as in Regimen B, and intrathecal MTX, ARA-C, CF and HC.

STRATIFICATION BY: First remission duration; site of relapse: bone marrow vs. EMD vs. both; participating institutions.

SPECIAL STUDY PARAMETERS: Bone marrow biopsy; organ measurements: liver, spleen, lymphnodes, testis; FBS; surface marker studies.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 52 patients will be entered within 2 years.

DOSAGE SCHEDULE:

Induction. Give a minimum of two courses.

Regimen A: VAP: VCR - 2.0 mg/sqm iv push on days 1, 8, 15 (maximum 2.0 mg/dose); ADR - 30 mg/sqm (maximum dose 450 mg/sqm) iv push on days 1, 2, 3; PRED - 60 mg/sqm/day po in 3 divided doses (maximum 60 mg/day) for 21 days. Repeat course on day 22 (ADR on days 22 to 24 or days 29 to 31, Revision 08/79) if bone marrow is M1 or M2 and granulocyte count is above 1000, then taper PRED over 7 days.

Regimen B: Enter patients with M3 status following Regimen A. TG - 100 mg/sqm po followed in 12 hours by ARA-C - 100 mg/sqm sc on days 1 through 5. Repeat every 15 days. Remove from study nonresponders (NR) or patients with progression after 3 courses.

Maintenance.

Arm I: On days 43 through 46 give TA: TG - 100 mg/sqm po followed in 12 hours by ARA-C - 100 mg/sqm sc. On day 64 begin COAP: VCR - 2.0 mg/sqm iv push on day 1 (maximum 2 mg); plus give ARA-C, CTX - each 35 mg/sqm iv push q 8 hours for 12 doses, and PRED - 35 mg/sqm po q 8 hours for 12 doses. Repeat alternate courses of TA/COAP q 21 days.

CNS Prophylaxis: Begin on day 64 or at time of first course of COAP.

MTX - 15 mg/sqm it (15 mg maximum) followed by HC - 30 mg/sqm it followed by ARA-C - 60 mg/sqm it (60 mg maximum) followed by CF - 15 mg/sqm im or iv. Repeat course q 4-5 days, twice weekly, for 4 courses. Give at 3-, 6-, and 9-week intervals.

Arm II: Beginning on day 127, give alternating TA/COAP, plus CNS prophylaxis, as in Arm I, followed by VAP as in Induction Regimen A. Taper PRED over 7 days to be discontinued on day 28 of course. Omit VAP therapy after maximum dose of ADR has been given.

Remove from study patients with M-3 marrow, persistent M-2 marrow, or proven CNS or EMD following Induction.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PRED - 5 mg tablets; HC - 100 mg vials; VCR - 1 and 5 mg vials; MTX - 20 and 50 mg vials; CTX - 100, 200, and 500 mg vials; ARA-C - 100 mg vials; ADR - 10 and 50 mg vials; TG - 40 mg tablets; CF - 3 mg ampules.

DATE SUMMARIZED: 07/79

6.0016 PHASE III SYSTEMIC AND CNS THERAPY, WITH VCR, PRED, L-ASP, ADR, ARA-C, TG, MTX, CTX, HC, AND RADIATION FOR T-CELL ALL IN CHILDREN

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PROTOCOL NUMBER(S) SWOG-7837

OBJECTIVES:

I. Evaluate the effectiveness of sequential systemic and intrathecal chemotherapy with vincristine (VCR), prednisone (PRED), L-asparaginase (L-ASP), adriamycin (ADR), cytosine arabinoside (ARA-C), 6-thioguanine (6-TG), methotrexate (MTX), cyclophosphamide (CTX), and hydrocortisone (HC), plus CNS radiotherapy for occult leukemia in children with untreated T cell acute lymphatic leukemia.

II. Assess the therapeutic effectiveness, as measured by disease-free survival, of SWOG #7837 vs. SWOG #7615 in treating children with T cell acute lymphatic leukemia.

III. Compare the value of cranial radiation therapy plus intrathecal chemotherapy every eight weeks (bimonthly) vs. only bimonthly intrathecal methotrexate in treating occult T cell leukemia of the central nervous system, using the rate of CNS relapse and the rate of CNS complications for comparison.

IV. Assess the toxicity, rate of complications, and type of relapse encountered by patients treated on SWOG #7837 vs. those treated on SWOG #7615.

PROTOCOL ENTRY CRITERIA: Patients less than 21 years of age with a diagnosis of T-cell acute lymphatic leukemia as defined by SWOG-7615 protocol including patients with 20% or greater E rosetting leukemia cells. Patients must have had no therapy prior to E rosette determination and one week or less of corticosteroid therapy thereafter.

PROTOCOL OUTLINE: Nonrandomized study. Randomize patients to SWOG-7615 or SWOG-7837 (this study) on a 1 to 4 basis, respectively.

Induction: Regimen A: 1 or 2-Drug Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574 plus Prednisone, PRED, NSC-10023; add L-Asparaginase, L-ASP, NSC-109229 if M1 marrow is not achieved by VCR/PRED.

Consolidation: Regimen B: 4-Drug Combination Chemotherapy plus Hormone Therapy, plus Intrathecal (IT) CNS Chemotherapy plus Cranial Radiotherapy. Adriamycin, ADR, NSC-3053; L-ASP; Cytosine arabinoside, ARA-C, NSC-63878; 6-Thioguanine, 6-TG, NSC-752; PRED; plus intrathecal Methotrexate, MTX, NSC-740; Hydrocortisone, HC, NSC-10483; and ARA-C plus CNS Radiation with megavoltage equipment.

Maintenance: Regimen C: Sequential 7-Drug Combination Chemotherapy and Hormone Therapy, plus (IT) 2-Drug Combination Chemotherapy and Hormone Therapy. VCR, ADR, PRED plus MTX, VCR plus Cyclophosphamide, CTX, NSC-26271; plus ARA-C, 6-TG and (IT) MTX, ARA-C and HC.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Liver and kidney function tests, SMA 12 and SMA 60, amylase, IVP and CNS studies.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, disease-free interval, CNS complications, recurrence rate.

CURRENT STATUS: 25 patients will be entered per year for 2.5 to 3 years.

DOSAGE SCHEDULE:

Induction: Regimen A: Give one 4 or 6 week course. VCR - 2.0 mg/sqm/week iv; PRED - 60 mg/sqm/day in 3 or 4 divided doses po. Enter consolidation after 4 weeks if M1 marrow is achieved; otherwise continue therapy for 2 weeks with addition of L-ASP - 10, 000 IU/sqm/week iv coinciding with VCR dose.

Consolidation: Regimen B: ADR - 60 mg/sqm iv on day 29 if marrow M-1 or on day 43 when M1 or M2 marrow is obtained; L-ASP - 10,000 IU/sqm/week for two weeks beginning same day as ADR; PRED - 30 mg/sqm/day in 3 or 4 divided doses beginning on same day as ADR for next 4 weeks, then taper dose to discontinue in 7 days; ARA-C - 100 mg/sqm/day iv or sc for 5 days beginning 4 weeks after beginning consolidation; 6-TG - 50 mg/sqm po for 5 days to 12 hours following ARA-C dose. IT Therapy. Give q 7 days for 4 weeks: MTX - 15 mg/sqm; HC - 15 mg/sqm and ARA-C - 30 mg/sqm. CNS Radiation - 2400 rads in 2.5 weeks in 5 fractions/week, 180 to 200 rads/dose through opposing lateral fields.

Maintenance: Regimen C: Change systemic therapy q 2 to 4 weeks sequentially for 12 weeks, and give bimonthly (IT) Chemotherapy. Continue for 3 years or until an M3 marrow is identified. Treat extramedullary relapse according to active SWOG protocol for rescue therapy. VCR - 2.0 mg/sqm iv on day 1; PRED - 60 mg/sqm for 14 days in 3 or 4 divided doses/day then stop without tapering; ADR - 40 mg/sqm iv on same day as VCR excluding first course. After the first 2 week course, add during the second and fourth courses MTX - 3.0 mg/kg iv; VCR - 2.0 mg/sqm iv on day 1 of each 2 week course. The third course consists of CTX - 800 mg/sqm iv on day 1. For the 4 weeks of maintenance, give ARA-C - 150 mg/sqm q other day (M, W, F) iv or sc; 6-TG - 50 mg/sqm po 8 to 12 hours following ARA-C; plus (IT) Therapy: MTX; HC and ARA-C as in Regimen B q 8 weeks beginning in week 16 on the same day as CTX. Continue therapy for 3 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PRED - 5 mg tablets; HC - 100 mg vials; MTX - 50 mg vials; TG - 40 mg tablets; CTX - 100, 200 and 500 mg vials; ARA-C - 100 mg vials; L-ASP - 10,000 IU vials; ADR - 10 and 50 mg vials; VCR - 1 and 5 mg vials.

DATE SUMMARIZED: 11/79

6.0017 PILOT CONSOLIDATION, MAINTENANCE & CNS THERAPY WITH COMBINATIONS OF L-ASP, CTX, MTX, HC, ARA-C, 6-MP, PRED, ADR AND TG FOR PEDIATRIC ALL

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PROTOCOL NUMBER(S) SWOG-7866; SWOG-ALINC-13

OBJECTIVES:

I. Subgroup classification of ALL at the time of diagnosis using a variety of laboratory methods: (a) Utilize multiple special laboratory procedures at the time of diagnosis of ALL, attempting to subclassify cases of ALL into laboratory designated categories. The laboratory methodologies will be the same at all participating institutions and will have been perfected at each institution during the Pilot ALinC 13-Classification study (SWOG 7865) activated 5/12/78. (b) Utilize part of the laboratory subclassification data prospectively in assigning prognostic categories for treatment randomization. (c) Utilize all of the laboratory subclassification data in retrospective analysis for relationship to outcome (after the study is completed).

II. Utilize a variety of treatment regimens and compare eventual outcome as related to each treatment regimen and as related to subgroup laboratory classification results obtained at the time of diagnosis to determine which type of treatment is best for which type of patient: (a) Stratify patients into good-risk and poor-risk prognostic categories on the basis of prognostic determinants plus information obtained from Pilot ALinC 13-C. The final retrospective analysis will look at response in each treatment group in relation to the multiple clinical findings and laboratory results recorded at the time of diagnosis. (b) Induce remission in all patients by Vincristine (VCR) and Prednisone (PRED) therapy followed by (c) the most successful consolidation treatment regimen from ALinC 11 as the 'standard' arm: L-Asparaginase (L-ASP), Cyclophosphamide (CTX), Methotrexate (MTX) for the good-risk group or L-ASP and CTX in the poor-risk group and compare with this additional therapy during Maintenance, consisting of either: 6-Mercaptopurine (6-MP), MTX, PRED or 6-MP, MTX, PRED and intermittent high-dose MTX or 6-MP, MTX, PRED and intermittent high-dose MTX plus pulse CTX or 6-MP, MTX and pulses of VCR, Adriamycin (ADR), PRED; Cytosine arabinoside (ARA-C), PRED; 6-Thioguanine (6-TG), CTX and PRED. (d) Give intermittent courses of high-dose MTX to penetrate sanctuaries (such as the testis) and pulse CTX as part of maintenance therapy to provide additional protection against extramedullary relapse. (e) Test whether intermittent high-dose MTX given parenterally during Maintenance can obviate the need for extended intrathecal medicines for patients not receiving cranial irradiation. (f) Test whether better therapy for poor-prognosis patients can be achieved by superimposing pulses of a multiplicity of different agents into the basic 'standard' maintenance regimen.

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age with a diagnosis of disseminated lymphoid malignancy (ALL, ASL, AUL or lymphoma with marrow dissemination). Patients must have had no prior chemotherapy nor T or B markers on the lymphoblasts. Sample collection for SWOG-8765 must be completed before entry to study. Stratification into appropriate prognostic groups and achievement of M1 marrow on Induction therapy are required for registration to Maintenance.

PROTOCOL OUTLINE: Randomized study for Consolidation and Maintenance only.

Induction: Enter all patients.

Single-agent Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

CNS Therapy for patients with CNS disease at diagnosis. 2-Drug Combination Intrathecal (it) Chemotherapy plus Hormone Therapy. Methotrexate, MTX, NSC-740; Hydrocortisone, HC, NSC-10483; Cytosine arabinoside, ARA-C, NSC-109229. Do not randomize these to Maintenance but enter patients to Arm III.

Consolidation and Maintenance:

Randomize good-risk patients to Arm I, II or III. Randomize poor-risk patients to Arm I, III or IV. (Arms II and III closed as of September 1979; Arm IV closed February 1980.)

Arm I:

Consolidation:

3-Drug Combination Chemotherapy plus Intrathecal 2-Drug Combination Chemotherapy and Hormone Therapy. L-Asparaginase, L-ASP, NSC-109229; Cyclophosphamide, CTX, NSC-26271; MTX; plus (it) MTX, HC, ARA-C.

Maintenance:

2-Drug Combination Chemotherapy and Hormone Therapy plus CNS Therapy (it) as above. 6-Mercaptopurine, 6-MP, NSC-775; MTX; PRED plus (it) MTX, HC, ARA-C.

Arm II: (Arm closed September 1979.)

Consolidation:

Same as Arm I Consolidation.

Maintenance:

2-Drug Combination Chemotherapy and Hormone Therapy plus High-dose Single-agent Chemotherapy. 6-MP, MTX, PRED plus high-dose MTX plus rescue by Citrovorum factor, CF, NSC-3590.

Arm III: (Arm closed September 1979.)

Consolidation:

Same as Arm I Consolidation.

Maintenance:

2-Drug Combination Chemotherapy plus Hormone Therapy plus High-dose Single-agent Chemotherapy plus CNS Therapy plus pulses of Single-agent Chemotherapy. 6-MP, MTX, PRED, high-dose MTX iv; MTX, HC, ARA-C (it) plus CTX pulses.

Arm IV: (Arm closed February 1980.)

Consolidation:

2-Drug Combination Chemotherapy. L-ASP, CTX.

Maintenance:

2-Drug Combination Chemotherapy plus CNS Therapy plus pulses of Combination Chemotherapy plus Hormone Therapy. 6-MP, MTX, plus MTX, HC, ARA-C (it) plus pulses: VCR, Adriamycin, ADR, NSC-123127, PRED; ARA-C, PRED; 6-Thioguanine, TG, NSC-752, CTX, PRED.

STRATIFICATION BY: Participating institutions, risk groups according to SWOG-7623 (ALinC-12) criteria, classification on SWOG-7865 (Pilot ALinC 13-C).

SPECIAL STUDY PARAMETERS: Kidney function tests, liver function tests.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response.

CURRENT STATUS: 300 good-risk patients will be entered in 3 years; 189 poor-risk patients will be entered in 2 1/2 years. (Arms II and III closed as of September 1979; Arm IV closed as of February 1980.)

DOSAGE SCHEDULE:

Induction:

PRED - 60 mg/sqm/day po in 3 or 4 divided doses (20 mg/day minimum; 60 mg/day maximum). After 4 weeks, if marrow is M1 decrease dosage: 50% on days 1 through 3; 50% on days 4 through 7. Discontinue PRED after 7 days. VCR - 2 mg/sqm iv (maximum dose 2 mg) for a minimum of 4 weeks, then if bone marrow is M1, randomize patients to Maintenance. If not M1, continue treatment another 2 weeks. If M1 marrow is not achieved, remove patients (NR) from study. Intrathecal therapy: MTX - 15 mg/sqm (maximum dose 15 mg); HC - 15 mg/sqm (maximum dose 15 mg); ARA-C - 30 mg/sqm (maximum dose 30 mg). Give each drug in sequence twice weekly until CSF is free of blasts. Remove nonresponders (NR) from study. If CNS and marrow response are achieved enter these patients to Arm III Maintenance.

Consolidation and Maintenance:

Arm I:

Consolidation:

Begin therapy on day 29. L-ASP - 6000 IU/sqm/day im or iv on days 29 through 43; CTX - 1000 mg/sqm iv on day 30 in a.m. and day 43 in a.m. Begin CNS therapy as in Induction on day 1 of 9th week (day 57) and repeat q 2 weeks for 6 courses; plus give MTX - 15 mg/sqm iv on days 58 through 61; repeat this 4-day MTX-iv course following MTX-it q 2 weeks for 6 courses.

Maintenance:

Begin on 21st week. 6-MP - 50 mg/sqm/day po; MTX - 20 mg/sqm po q 7 days (omit when MTX (it) is given); PRED - 60 mg/sqm/day po in 4 divided doses for 28 days followed by 7 days of decremental therapy. Give PRED q 16 weeks for 3 years. Begin CNS therapy (it) on 25th week and give q 8 weeks for 3 years.

Arm II:

Consolidation:

As in Arm I.

Maintenance:

Begin on 21st week. 6-MP; MTX (po) and PRED, as in Arm I, followed beginning in week 25 by high-dose MTX - 1000 mg/sqm iv in a one-hour drip, with adequate hydration followed by CF - 30 mg/sqm po q 6 hours after MTX infusion and repeated q 6 hours for 2 doses. Omit MTX (po) on day high-dose MTX is given. Omit CNS therapy.

Arm III:

Consolidation:

As in Arm I.

Maintenance:

Begin on 21st week. 6-MP; MTX (po) and PRED as in Arm I; high-dose MTX iv as in Arm II beginning in week 25 and concomitantly with each course of CNS intrathecal therapy; CTX - 800 mg/sqm iv push beginning in week 29 and repeated q 8 weeks for 3 years. Omit scheduled MTX po on day CTX is given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

6.0018 PHASE III RESCUE THERAPY FOR NON-CNS EXTRAMEDULLARY DISEASE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-7901

OBJECTIVES:

I. Administer effective local therapy for non-CNS extra medullary disease (EMD).

II. Determine the effects of re-Induction and Maintenance by the next priority bone marrow remission Induction protocol, by CNS reinforcement therapy and local radiotherapy for non-CNS EMD in children with acute lymphoblastic leukemia who are in: (1) bone marrow and CNS remission; (2) bone marrow relapse and CNS remission; (3) CNS relapse and bone marrow remission; (4) bone marrow and CNS relapse.

III. Accumulate data on relative incidence and prognostic implications of non-CNS EMD at various sites.

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age at time of diagnosis of acute lymphoblastic leukemia with tissue or cytologically confirmed (except for intraocular and mediastinal) non-CNS EMD. Patients must be under the care of a Pediatric SWOG Investigator.

PROTOCOL OUTLINE: Nonrandomized study. Enter all patients to Regimens A and B.

Regimen A: Chemotherapy. Appropriate SWOG protocols.

Regimen B: Radiotherapy. Supervoltage, according to site of EMD.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: IVP, CSF tests, bone survey.

END POINTS: Response/remission rate, duration of response, survival time, time from EMD to marrow relapse or to second relapse.

CURRENT STATUS: 37 patients will be entered for each EMD site.

DOSAGE SCHEDULE:

Regimen A: Remove all patients from current bone marrow Maintenance protocol and enter on current SIMAL protocol. Give patients not eligible for current SIMAL next priority systemic Induction and Maintenance therapy for which they are eligible. Give CNS Induction and Maintenance reinforcement therapy according to currently active SIMAL protocol to patients in CNS remission: and give CNS therapy according to current CNS leukemia protocol to patients in CNS relapse.

Regimen B: Radiotherapy according to EMD site: testicles and mediastinum - 2600 rad in 13 fractions: renal - 1700 rad over 3.5 weeks; ocular and single mass bone lesions - 2600 rad; diffuse bone lesions - 1000 to 5000 rad in 2 or 3 fractions to involved areas.

Remove patients from study when bone marrow relapse occurs. Reenter patients with new or recurrent EMD.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/79

6.0019 PHASE III EVALUATION OF TWO COMBINATION CHEMOTHERAPY/HORMONE THERAPY REGIMENS FOR MAINTENANCE IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-8001

OBJECTIVES:

I. Evaluate the effectiveness, in terms of complete remission rate, of the L10 protocol using vincristine/prednisone/adriamycin for Induction followed by intensive Consolidation with methotrexate/cytosine arabinoside/6-thioguanine/it methotrexate/vincristine/prednisone/L-asparaginase/cyclophosphamide in adults with acute lymphoblastic leukemia.

II. Compare two Maintenance regimens for their effects on remission duration and survival: successive courses of POMP (prednisone/vincristine/methotrexate/6-mercaptopurine), COAP (cyclophosphamide/vincristine/cytosine arabinoside/prednisone), and OPAL (vincristine/prednisone/adriamycin/L-asparaginase) vs. the L10 'eradication' regimen.

III. Determine the reproducibility of the FAB histologic classification and correlation to response to therapy of acute lymphoblastic leukemia in adults.

PROTOCOL ENTRY CRITERIA: Patients with acute lymphoblastic leukemia who have an absolute infiltration of the marrow of greater than 50 percent blasts or those with an absolute infiltration of 30-49 percent who also have progressive disease prior to entry. Patients must be at least 15 years old and may not have had prior chemotherapy. There must be no serious hypertension, significant abnormality of the EKG, or other indication of cardiac disease. Liver and kidney function should be adequate.

PROTOCOL OUTLINE: Study randomized for Maintenance only.

Regimen A: Induction. 4-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740; Cyclophosphamide, CTX, NSC-26271; Prednisone, PRED, NSC-10023.

Regimen B: Consolidation. 6-Drug Combination Chemotherapy plus Hormone Therapy. MTX; Cytosine arabinoside, ARA-C, NSC-63878; 6-Thioguanine, TG, NSC-752; VCR; L-Asparaginase, L-ASP, NSC-109229; CTX; PRED.

Maintenance. Randomize to Arms I and II.

Arm I: Multi-Drug Sequential Combination Chemotherapy plus Hormone Therapy. POMP: PRED; VCR; MTX; 6-Mercaptopurine, 6-MP, NSC-755; followed by COAP: CTX; VCR; ARA-C; PRED; followed by OPAL: VCR; PRED; ADR; L-ASP.

Arm II: Multi-Drug Combination Chemotherapy plus Hormone Therapy. PRED; ADR; 6-MP; MTX; Actinomycin-D, ACT-D, NSC-3053; VCR; BCNU, NSC-409962; CTX.

STRATIFICATION BY: Participating institutions, age (above or below 50), blast characteristics (L1 vs. L2-null vs. L2-B or T vs. L3).

SPECIAL STUDY PARAMETERS: Performance status, hemogram, liver and kidney function tests, EKG, bone marrow.

END POINTS: Response/remission rate, duration of response, recurrence rate, survival.

CURRENT STATUS: At least 52 patients will be entered into the Maintenance arms over 2 years.

DOSAGE SCHEDULE:

Regimen A: Induction. VCR - 2 mg/sqm (dose not to exceed 4 mg in patients under 60 and 2.5 mg in patients over 60) iv on days 1, 8, 15, 22, and 29; PRED - 60 mg/sqm/day po in 3 divided doses on days 1 through 36, then tapering over 7 days; ADR - 20 mg/sqm (total cumulative dose not to exceed 450 mg/sqm) iv on days 17, 18, and 19; MTX - 6 mg/sqm it on days 3, 5, 15, 34, and 36 if platelet count is at least 50,000 and BUN is less than 20 mg percent; CTX - 600 mg/sqm iv push on day 36; ADR - 30 mg/sqm iv push on day 36. An Ommaya reservoir will be implanted in the frontotemporal area of the skull on or about day 30 in patients with an initial WBC of more than 20,000 and who achieve an A1 marrow status. If A1 marrow status is not achieved by then, placement of the reservoir is delayed until after CTX and ADR are given, on or about day 50.

Regimen B: Consolidation. Beginning after 14-day rest period following CTX and ADR. MTX - 15 mg/sqm (total dose not to exceed 25 mg) iv on days 1 through 5 of Consolidation; repeat on days 36 and 71; ARA-C - 200 mg/sqm/day by continuous iv infusion on days 1 through 5 and repeated on days 36 and 71; TG - 120 mg/sqm iv q 12 hours for 12 doses, beginning on days 15, 50, and 85; MTX - 6 mg/sqm it on days 15, 17, 57, and 59; VCR - 1.4 mg/sqm (not greater than 2 mg) iv on days 50 and 57; PRED - 60 mg/sqm/day po for 7 days beginning on day 50; L-ASP - 60,000 IU/sqm iv 3 times weekly for a total of 6 doses, beginning on day 99; CTX - 1200 mg/sqm iv on day 110, following the last dose of L-ASP. Begin Maintenance after a 2-week rest.

Arm I: Maintenance. Give 3 courses of POMP followed by 3 courses of COAP followed by 3 courses of OPAL, all courses repeating q 4 weeks. POMP: PRED - 100 mg/day po on days 1 through 5; VCR - 1 mg iv on day 1; MTX - 7.5 mg/sqm iv on days 1 through 5; 6-MP - 500 mg/sqm iv on days 1 through 5. COAP: CTX - 75 mg/sqm iv on days 1 through 5; VCR - 1 mg iv on day 1; ARA-C - 75 mg/sqm/day sc in 4 divided doses q 6 hours on days 1 through 5; PRED - 100 mg/day po on days 1 through 5. OPAL: VCR - 1 mg iv on day 1; PRED - 100 mg/sqm po on days 1 through 5; ADR - 40 mg/sqm iv on day 1; L-ASP - 20,000 IU iv twice weekly for a total of 6 doses, then omit L-ASP from all subsequent courses of Chemotherapy. Two doses of it MTX at 6 mg/sqm are given on alternate days starting with the second course of Maintenance; the same two doses are repeated q 3 months thereafter. Continue Maintenance for 36 months or until relapse.

Arm II: L10 Maintenance therapy. VCR - 1 mg/sqm iv on days 1 and 8; PRED - 90 mg/sqm po q 12 hours for 7 days beginning 8-12 hours after the first dose of VCR; ADR - 20 mg/sqm iv on days 15, 16, and 17; 6-MP - 90 mg/sqm/day po on days 36 through 65; MTX - 6 mg/sqm it on days 36 and 38; MTX - 20 mg/sqm po on days 43, 50, 57, 64, 113, 120, 127, and 134; ACT-D - 1000 micrograms/sqm iv on days 71 and 147; VCR - 1 mg/sqm iv on days 78 and 85; PRED - 90 mg/sqm/day po on days 78 through 84; BCNU - 80 mg/sqm iv on day 92; CTX - 800 mg/sqm iv on day 92; 6-MP - 90 mg/sqm/day po on days 106 through 135; MTX - 6 mg/sqm it on days 106 and 108. Repeat q 21 weeks for 36 months or until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg ampules; PRED - 5 and 50 mg tablets; ADR - 10 and 50 mg vials; CTX - 100, 200, and 500 mg ampules and 50 mg tablets; MTX - 50 mg vials; ARA-C - 100 and 500 mg vials; TG - 50 mg tablets; L-ASP - 10,000 IU vials; 6-MP - 500 mg vials and 50 mg tablets; ACT-D - 0.5 mg vials; BCNU - 100 mg vials.

DATE SUMMARIZED: 08/80

6.0020 PHASE III INDUCTION WITH MOAD (MTX/VCR/L-ASP/DM) PLUS 6-MP, ADR, ARA-C, AND TG FOR ADULT ACUTE LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) BCRP-7508

OBJECTIVES:

I. Improve the remission induction rate in adult patients with acute lymphocytic leukemia by utilizing vincristine and dexamethasone with intermittent moderate doses of methotrexate followed by L-asparaginase.

II. Decrease the incidence of severe infections during induction therapy by utilizing oral nonabsorbable antibiotics.

III. Determine whether intermittent high-dose methotrexate with vincristine and dexamethasone will prolong remission duration in a significant percentage of these patients.

IV. Determine the efficacy of moderate and high-dose methotrexate in preventing meningeal leukemia and correlate clinical effectiveness with the concentration of methotrexate in the CSF.

PROTOCOL ENTRY CRITERIA: Previously untreated patients, age 15 years and over, with a diagnosis of acute lymphocytic leukemia. Patients may have had up to 13 days of prior corticosteroid therapy. No patients with active infection should be entered prior to instituting antibiotic treatment and general supportive measures. Patients with hyperuricemia and elevated BUN should be treated with diuresis and allopurinol to normalize these parameters prior to entry. Patients with meningeal leukemia will be treated for this while being entered on the protocol.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Induction. 4-Drug Combination Chemotherapy. MOAD: Methotrexate, MTX, NSC-740; Dexamethasone, DM, NSC-34521; Vincristine, VCR, NSC-67574; L-asparaginase (E. coli), L-ASP, NSC-109229.

Regimen B: Consolidation. 2-Drug Combination Chemotherapy. MTX; L-ASP.

Regimen C: Cytoreduction. 3-Drug Combination Chemotherapy. VCR; DM; MTX; Citrovorum Factor, CF, NSC-3590.

Regimen D: Maintenance. 4-Drug Combination Chemotherapy. VCR; DM; MTX; 6-Mercaptopurine, 6-MP, NSC-755.

Regimen E: Reinduction. 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cytosine arabinoside, ARA-C, NSC-63878.

Regimen F: Maintenance. 2-Drug Combination Chemotherapy. 6-Thioguanine, TG, NSC-752; ARA-C.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, bone marrow biopsy and aspiration, CEA, CSF cytologic studies and MTX level.

END POINTS: Response/remission rate, duration of response, recurrence rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: MOAD: MTX - 100 mg/sqm iv push on day 1. Increase subsequent doses to minimal toxicity by 50 percent each course to 225 mg/sqm, thereafter by 25 percent each course; DM - 6 mg/sqm/day po for 10 days; VCR - 2 mg iv push on day 2; L-ASP - 500 IU/kg by 30-minute iv infusion on day 2, 24 hours after MTX. Repeat courses to be given on days 11, 21, etc. Patients who do not show evidence of marrow improvement after 3 courses go off study. Patients with CR must receive a minimum of 5 courses, the last 2 of which must be given after attainment of CR. Enter CR to Regimen B immediately.

Regimen B: MTX - continue at established tolerable dose or increase by 25 percent each course to minimal toxicity, iv push on day 1; L-ASP - 500 IU/kg iv infusion over 30 minutes on day 2. Continue at 10-day intervals for a total of 6 courses. Enter patients in CR to Regimen C.

Regimen C: VCR - 2 mg iv push on day 1; DM - 6 mg/sqm po on days 2 through 6; MTX - 100 mg/kg steady 6-hour iv infusion beginning 30 minutes after VCR on day 1, increasing each subsequent dose by 25 percent to minimal toxicity; CF - 1.67 percent of the MTX dose (mg/mg)/day for 3 days beginning 2 hours after the end of the MTX infusion, by continuous iv infusion for the first 48 hours and in 4 divided oral doses on the third day. Repeat course monthly for 12 courses. Enter all patients in CR at the end of Regimen C to Regimen D.

Regimen D: VCR - 2 mg iv push on day 1; DM - 6 mg/sqm/day po on days 1 through 5; MTX - 15 mg/sqm/week po adjusted to minimal bone marrow or mucosal toxicity; 6-MP - 100 mg/sqm/day po adjusted to minimal bone marrow toxicity. Repeat course at 4-week intervals indefinitely until bone marrow relapse. At relapse enter patients to Regimen E.

Regimen E: ADR - 60 mg/sqm iv push on day 1; ARA-C - 100 mg/sqm/day by continuous iv infusion on days 1 through 7. VCR and DM should be added if relapse occurs during or just after consolidation therapy is finished. Course to be repeated at least once. Enter patients with bone marrow remission to Regimen F.

Regimen F: 6-TG - 100 mg/sqm/day po on days 1 through 5; ARA-C - 100 mg/sqm/day iv push on days 1 through 5. Repeat course in 1 month then alternate one course of Regimen E at monthly intervals with 2 courses of Regimen F. Continue until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

6.0021 COMBINATION CHEMOTHERAPY WITH PREDNISOLONE, VCR, AND L-ASP FOR REINDUCTION OF REMISSION IN ACUTE LYMPHOCYTIC LEUKEMIA IN CHILDREN

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PROTOCOL NUMBER(S) MDAR-201; MDA-P-7730n

OBJECTIVES:

I. Evaluate hepatic function in patients receiving a combination of prednisolone, vincristine and L-asparaginase compared to historical controls using prednisolone.

II. Evaluate the remission induction effectiveness of a drug combination of the above agents compared to historical experience using prednisolone.

III. Compare the effectiveness of two dosage levels of prednisolone.

PROTOCOL ENTRY CRITERIA: Patients less than 21 years of age with acute lymphocytic leukemia in bone marrow relapse who do not have overt diabetes, pancreatitis or history of prior L-asparaginase toxicity.

PROTOCOL OUTLINE: Randomized study. Randomization will be for dosage difference only.

Arm I and Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; L-Asparaginase, NSC-109229; plus Prednisolone, PRDL, NSC-9900.

STRATIFICATION: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity or treatment, survival rate, length of survival.

CURRENT STATUS: 100 patients will be entered in approximately 3 years.

DOSAGE SCHEDULE:

Arm I: PRDL - 40 mg/sqm/day po; VCR - 2.0 mg/sqm iv; L-ASP - 500 IU/sqm iv on days 1 through 15.

Arm II: PRDL - 60 mg/sqm/day po; VCR; L-ASP - as in Arm I.

Length of courses and number of courses to be given are not stated.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/78

6.0022 IMMUNOTHERAPY WITH C. PARVUM PLUS COMBINATION CHEMOTHERAPY WITH CHOPBLEO FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN ADULTS

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PROTOCOL NUMBER(S) MDAR-203; MDA-DT-7703

OBJECTIVES:

I. Improve the remission induction rate in acute lymphocytic leukemia.

II. Prolong the duration of survival and complete remission.

III. Assess the efficacy of immunotherapy in this disease.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with acute lymphoblastic, undifferentiated and hairy cell leukemia, as well as patients with leukemic conversion of lymphoma who have not received more than 2 weeks of therapy with adriamycin, cyclophosphamide or bleomycin.

PROTOCOL OUTLINE: Nonrandomized study.

Induction-Consolidation:

Immunotherapy plus 4-Drug Combination Chemotherapy plus Hormone Therapy. Corynebacterium parvum, C. parvum; plus CHOP BLEO: Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066; Prednisone, PRED, NSC-10023.

Maintenance:

Sequential 3-Drug Combination Chemotherapies plus Hormone Therapy. COAP: CTX; VCR; Cytosine arabinoside, ARA-C, NSC-63878; PRED; followed by OPAL: VCR; ADR; L-Asparaginase, L-ASP, NSC-109229; PRED; followed by POMP: 6-Mercaptopurine, 6-MP, NSC-755, VCR; MTX; PRED.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: 100 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Induction-Consolidation:

C. parvum - 0.25 mg/sqm/day for 4 days (maximum cumulative dose per course is 2.5 mg/sqm) to begin 4 days prior to start of Chemotherapy; in patients whose circulating white cell count is less than 30,000, CHOPBLEO: ADR - 60 mg/sqm iv on day 1; CTX - 1, 000 mg/sqm iv on day 1; VCR - 2 mg iv on days 1 and 7; BLEO - 5 mg given 6 hours after each dose of VCR; PRED - 100 mg/day in 4 divided doses for 10 days. Number of C. parvum-CHOPBLEO induction courses given depends on patient's hematological status. Give 3 additional complete courses for Consolidation.

Maintenance:

Enter all patients to 3 courses of COAP, followed by 3 courses of OPAL, followed by 3 courses of POMP. No details of dosage schedule given. Continue therapy for 2 years.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/78

6.0023 INDUCTION AND MAINTENANCE WITH VINCRISTINE/PREDNISONE/METHOTREXATE FOR CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) MDAR-250; MDA-P-7738n

OBJECTIVES:

I. Determine the efficacy of high dose methotrexate (MTX)/vincristine (VCR)/prednisone (PRED) for Induction and Maintenance in childhood acute lymphocytic leukemia.

PROTOCOL ENTRY CRITERIA: Patients with acute lymphocytic leukemia. Patients must be under 21 years of age with adequate hepatic function. Patients must be in bone marrow relapse after prior therapy or enter Maintenance after alternative induction.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; Methotrexate, MTX, NSC-740.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Duration of response, response/remission rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: VCR - 2 mg/sqm iv on days 1, 7, 14 and 21; PRED - 60 mg/sqm po in 3 divided doses on days 1 through 28; MTX - 3 mg/kg iv followed by 2 mg/kg iv drip on days 1 and 15.

Maintenance: VCR - 2 mg/sqm iv on day 1; PRED - 40 mg/sqm po in 3 divided doses on days 1 through 15; MTX - 3 mg/kg iv followed by 2 mg/kg iv drip on day 1. Repeat course q 21 days. Adjust systemic MTX dosage if MTX is also given intrathecally for CNS prophylaxis or therapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

6.0024 MULTIPLE-AGENT CHEMOTHERAPY FOR THE INDUCTION, CONSOLIDATION AND MAINTENANCE OF ADULT ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) MSKCC-7339

OBJECTIVES:

I. Increase the remission rate and prolong the remission and ultimately the survival of patients with acute lymphoblastic leukemia.

II. Study the efficacy of intraventricular acute leukemia agents in the prophylaxis of CNS leukemia for cases of patients with high wbc on presentation.

III. Eradicate, if possible, all leukemic cells in the human host with the overall purpose of 'curing' acute leukemia.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with acute lymphoblastic leukemia, previously untreated, or with only minimal prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740; plus Prednisone, PRED, NSC-10023.

Consolidation: 5-Drug Combination Chemotherapy. MTX; Cytosine arabinoside, ARA-C, NSC-63878; Thioguanine, TG, NSC-752; L-Asparaginase, L-ASP, NSC-109229, 106997; Cyclophosphamide, CTX, NSC-26271.

Maintenance, Sequence 1: 5-Drug Combination Chemotherapy plus Hormone Therapy. VCR; ADR; MTX; 6-Mercaptopurine, 6-MP, NSC-755; Actinomycin-D, ACT-D, NSC-3053; plus PRED.

Maintenance, Sequence 2: 6-Drug Combination Chemotherapy plus Hormone Therapy. VCR; MTX; CTX; 6-MP; ACT-D; BCNU, NSC-409962; plus PRED.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: SMA-12, 5-nucleotidase, periodic re-evaluation of patient's surface area.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: VCR - 1.5 to 2.0 mg/sqm iv (maximum 4.0 mg) on days 1 and 7. Evaluate marrow on day 14. For patients who achieve M1 status, administer a third dose of VCR followed 2 days later (on day 16) by ADR - 20 mg/sqm/day iv on days 16, 17 and 18. For patients who do not achieve M1, repeat VCR for a third dose and reevaluate in 7 days, delaying ADR until days 23, 24 and 25. Give subsequent doses of VCR on days 21 and 28 if M1, or on days 28 and 35 if M1 not demonstrated on day 14. Give MTX - 6.25 mg/sqm it on days 3, 5, 16, 18, 26 and 28, if platelet count is over 50,000 and BUN is below 20 mg%. Give PRED - 60 mg/sqm/day po in 3 divided doses to begin 8 to 12 hours following initiation of VCR, to continue to the day of the last dose of VCR, then taper in 4 to 7 days. Allow a 10-day recovery period following the last dose of VCR, and proceed to Consolidation. If initial wbc is over 20,000 and M1 marrow is achieved, place Omaya reservoir in the fronto-temporal area of the skull on or about day 35.

Consolidation: MTX - 15 mg/sqm/day iv (maximum 25 mg) for 5 days starting on day 40, repeating on days 76 and 110; ARA-C - 300 mg/sqm/day iv and TG - 240 mg/sqm/day po, each in 2 divided doses for 6 to 10 days depending on tolerance, beginning on day 54, and repeated on days 90 and 124; L-ASP - 60,000 IU/sqm iv 3 times a week for 6 weeks to commence immediately following the third course of ARA-C/TG; CTX - 1200 mg/sqm iv on day 146. For patients who have an initial wbc of less than 20,000/cumm and have not had placement of an Omaya reservoir, administer MTX - 6.25 mg/sqm it on days 54, 56, 90 and 92. Rest 10 days after each course of MTX and two weeks after the first 2 courses of ARA-C and TG, and after CTX course, then proceed to Maintenance, Sequence 1.

Maintenance, Sequence 1: VCR - 2.0 mg/sqm iv for 2 doses administered 7 days apart followed 7 days after the second dose by ADR - 20 mg/sqm iv for 3 days. Allow a 2-week rest period then administer 6-MP - 90 mg/sqm/day po for 30 days; MTX - 20 mg/sqm po q 5 to 7 days for 4 to 5 doses to begin on the fourth day of 6-MP; ACT-D - 1000 gamma/sqm iv to begin 7 days following completion of 6-MP therapy; plus PRED - 180 mg/sqm/day in 2 divided doses for 7 days to begin 8 to 12 hours after initiation of VCR. For patients with platelet counts greater than 50,000/cumm, also give MTX - 6.25 mg/sqm it on days 1 and 3 of the 6-MP cycle. Rest 7 days and proceed to Maintenance, Sequence 2.

Maintenance, Sequence 2: VCR; 6-MP; MTX; ACT-D; PRED - as in Sequence 1; BCNU - 80 mg/sqm iv concurrent with CTX - 800 mg/sqm iv to follow completion of VCR. Upon completion of this entire sequence, return to Sequence 1 and continue to alternate the two Maintenance sequences for a period of one year.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/78

6.0025 CYCLIC COMBINATION CHEMOTHERAPY WITH ADR/VCR/PRED/6-MP/MTX FOR RECURRENT CHILDHOOD LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) SJCRH-R-7

OBJECTIVES:

I. Determine the therapeutic efficacy of aggressive second continuation chemotherapy with 2-drug combinations after reinduction with adriamycin/prednisone/vincristine in children with acute lymphocytic leukemia who relapse after elective cessation of therapy.

II. Evaluate the toxicity associated with this treatment.

III. Determine the histopathologic incidence of testicular leukemia in boys who relapse during unmaintained remissions and compare it with the incidence of gonadal disease at the time therapy is first stopped.

IV. Determine whether absorption of orally administered methotrexate is affected by the concomitant prophylactic administration of sulfamethoxazole-trimethoprin therapy.

PROTOCOL ENTRY CRITERIA: Children with acute lymphocytic leukemia who develop recurrent disease following elective cessation of initial therapy. Patients may have exclusively hematologic relapses or disease may be present in the CNS and/or testes.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with evidence of testicular leukemia to Regimen A at time of reinduction.

Reinduction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590; plus Prednisone, PRED, NSC-10023.

Regimen A: Radiotherapy.

Continuation Therapy: 2-Drug Alternating Combination Chemotherapy plus Hormone Therapy. 6-Mercaptopurine, 6-MP, NSC-755; plus MTX; alternating with ADR; PRED; plus it MTX; alternating with VCR; Cyclophosphamide, CTX, NSC-26271.

Late Intensification Therapy: 3-Drug Combination Chemotherapy plus Hormone Therapy. ADR; VCR; MTX; plus PRED.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, coagulation screening, liver and kidney function tests, hepatitis B surface antigen, chest x-ray, EKG, echocardiogram, systolic time interval, pulmonary function tests, EEG, CT scans of the head, CSF examination, bone marrow aspiration, bilateral testicular biopsies.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 25 patients will be entered.

DOSAGE SCHEDULE:

Reinduction. ADR - 40 mg/sqm iv on days 1 and 15; VCR - 1.5 mg/sqm on days 1, 8, 15, 22; PRED - 40 mg/sqm/day po on days 1 through 28; MTX - 12 mg/sqm (maximum 12 mg) it q week beginning on the second week; CF - 3 mg po q 6 hours for 4 doses on the day following MTX. Children in CR on day 28 begin continuation therapy.

Regimen A: Radiotherapy - 2400 rads over 10-14 days to both gonads.

Continuation Therapy: 6-MP - 50 mg/sqm/day po for 6 weeks; MTX - 40 mg/sqm/week po for 6 weeks; repeat 6-MP/MTX courses on weeks 15-20, 29-34, 43-48, 56-61, and 68-73. PRED - 40 mg/sqm/day po for 1 week; ADR - 20 mg/sqm iv; MTX - 12 mg/sqm (maximum 12 mg) it; administer PRED/ADR/it MTX on week 7 and q 7 weeks thereafter through week 49, after which give only it MTX on weeks 56, 62, 68, and 74. VCR - 1.0 mg/sqm/week iv; CTX - 300 mg/sqm/week iv; give VCR/CTX in 6-week courses beginning on weeks 8, 22, 36, 50, 62, and 74. Patients who develop hematologic relapse during continuation therapy go off study. Those who remain in second CR after 18 months of continuation therapy proceed to late intensification.

Late Intensification Therapy. Identical to Reinduction Therapy. Cease all therapy after 4 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

6.0026 COMBINATION CHEMOTHERAPY WITH VM-26/ARA-C VS VCR/CTX FOR MAINTENANCE OF SECOND HEMATOLOGIC REMISSIONS OF CHILDHOOD LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) SJCRH-R-8

OBJECTIVES:

I. Compare prednisone/daunomycin/VM-26 vs. prednisone/daunomycin/vincristine as reinduction therapy in children with acute lymphocytic leukemia who developed first marrow relapse during initial therapy.

II. Compare Maintenance therapy with VM-26/cytosine arabinoside vs. vincristine/cyclophosphamide in these patients.

III. Study the biological characteristics of lymphoblasts at relapse.

PROTOCOL ENTRY CRITERIA: Children with acute lymphocytic leukemia who develop first marrow relapse during initial therapy. Relapse may be exclusively hematologic or may involve other sites as well.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I and II. Assign those with CNS disease to Regimen A simultaneously. After Intensification Therapy, enter patients who had been in Arm I to Regimen B and those from Arm II to Regimen C.

Remission Reinduction Therapy.

Arm I: 2-Drug Combination Chemotherapy plus Hormone Therapy. Daunomycin, DNM, NSC-82151; VM-26, NSC-122819; plus Prednisone, PRED, NSC-10023.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. DNM; Vincristine, VCR, NSC-67574; plus PRED.

Regimen A: 2-Drug Combination Intrathecal Chemotherapy. Methotrexate; MTX, NSC-740; Cytosine arabinoside, ARA-C, NSC-63878.

Intensification Therapy. 2-Drug Combination Chemotherapy. VM-26; ARA-C.

Maintenance Therapy.

Regimen B: 2-Drug Combination Systemic Chemotherapy plus 2-Drug Combination Intrathecal Chemotherapy. VM-26; ARA-C; plus MTX; ARA-C.

Regimen C: 2-Drug Combination Systemic Chemotherapy plus 2-Drug Combination Intrathecal Chemotherapy. VCR; CTX; plus MTX; ARA-C.

STRATIFICATION BY: CNS involvement at relapse (yes vs. no).

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, coagulation screening, chest x-ray, EKG, echocardiogram, CSF examination, bone marrow aspirations for cytology, DNA histograms, karyotype analysis, cell surface markers, drug resistance studies, and glucocorticoid receptors.

END POINTS: Response/remission rate, duration of response.

CURRENT STATUS: A minimum of 45 patients will be entered in 1.5 years.

DOSAGE SCHEDULE:

Arm I: PRED - 40 mg/sqm/day po for 28 days; DNM - 25 mg/sqm/week iv for 4 weeks; VM-26 - 165 mg/sqm/week iv for 4 weeks. Patients in remission at the end of 4 weeks enter Intensification. Those not in remission will be treated with 2 additional weeks of PRED plus VM-26 at the same dosages plus 2 weekly doses of VCR at 1.5 mg/sqm/week iv.

Arm II: PRED - 40 mg/sqm/day po for 28 days; DNM - 50 mg/sqm/week iv for 4 weeks; VCR - 1.5 mg/sqm/week iv for 4 weeks. Patients in remission after 4 weeks enter Intensification. Those not in remission will be treated with 2-4 weeks of reinduction therapy as in Arm I. Patients still not in remission after 8 weeks will receive 3 weekly courses of MTX (100 mg/sqm iv) followed in 24 hours by L-asparaginase (10,000 IU/sqm). Patients still not in remission will receive 3 courses of CTX (150 mg/sqm/day po for 7 days) plus adriamycin (35 mg/sqm on day 8) at 7- to 10-day intervals.

Regimen A: MTX - 10 mg/sqm it; ARA-C - 50 mg/sqm it; administer on weeks 2 and 5 and give 4 weekly it injections on weeks 2, 3, 4, and 5.

Intensification: VM-26 - 165 mg/sqm iv twice weekly for 2 weeks; ARA-C - 300 mg/sqm iv twice weekly for 2 weeks. After treatment, enter patients from Arm I to Regimen B and patients from Arm II to Regimen C.

Regimen B: VM-26 - 150 mg/sqm iv q 2 weeks; ARA-C - 300 mg/sqm iv q 2 weeks; MTX - 10 mg/sqm it q 6 weeks; ARA-C - 50 mg/sqm it q 6 weeks. Continue treatment until marrow relapse or until 30 months of second CR.

Regimen C: VCR - 1.0 mg/sqm/week; CTX - 300 mg/sqm/week; MTX - 10 mg/sqm it q 6 weeks; ARA-C - 50 mg/sqm it q 6 weeks. Continue treatment until marrow relapse or until 30 months of second CR.

If CNS leukemia develops during hematologic remission, administer it MTX (10 mg/sqm) and it ARA-C (50 mg/sqm) weekly for 4 weeks and thereafter monthly. Also reinforce systemic Chemotherapy with the addition of PRED (40 mg/sqm/day for 14 days) and DNM (25 mg/sqm/week).

If relapse occurs in the gonads, treatment will consist of local Radiotherapy (2400 rads over 10-14 days) and intensified systemic Chemotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

6.0027 TOTAL THERAPY OF CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA IN PATIENTS AT STANDARD RISK

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PROTOCOL NUMBER(S) SJCRH-TOT-105

OBJECTIVES:

I. Determine the effect of intermittent, high-dose iv methotrexate (MTX) on the duration of complete remission in children with acute lymphocytic leukemia induced with prednisone/vincristine/asparaginase/it MTX.

II. Determine the effect on CR duration of administration of pairs of drugs sequentially during Maintenance: 6-mercaptopurine plus MTX, followed by cyclophosphamide plus adriamycin, followed by VM-26 plus cytosine arabinoside, followed by 6-mercaptopurine plus MTX.

III. Compare two regimens for CNS prophylaxis: iv plus it MTX vs. cranial irradiation plus it MTX.

PROTOCOL ENTRY CRITERIA: Previously untreated children with acute lymphocytic leukemia whose initial WBC is less than 100,000 and who have E-rosette negative lymphoblasts. There must be neither a mediastinal mass nor CNS involvement.

PROTOCOL OUTLINE: Randomized study. Enter all patients on Regimen A for Induction, then randomize patients to Arms I and II for CNS prophylaxis. Then enter Arm I patients onto Arm III and Arm II patients onto Arm IV.

Induction.

Regimen A: 3-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; L-asparaginase, L-ASP, NSC-109229; it Methotrexate, MTX, NSC-740; plus Prednisone, PRED, NSC-10023.

CNS Prophylaxis.

Arm I: Single-agent Chemotherapy plus Leucovorin Rescue. MTX (iv, high-dose, and it); plus Citrovorum Factor, CF, NSC-3590.

Arm II: Single-agent Chemotherapy plus Radiotherapy. MTX, it; plus Co-60 irradiation.

Maintenance.

Arm III: 2-Drug Combination Chemotherapy plus Leucovorin Rescue. 6-Mercaptopurine, 6-MP, NSC-755; MTX (at conventional doses plus pulses of high-dose and it); plus CF.

Arm IV: 2-Drug Combination Sequential Chemotherapy. 6-MP; MTX; followed by Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; followed by VM-26, NSC-122819; Cytosine arabinoside, ARA-C, NSC-63878.

STRATIFICATION BY: Sex, age (5 years and under vs. 6-10 years vs. over 10 years), initial WBC (less than 10,000 vs. 10,000-25,000 vs. more than 25,000).

SPECIAL STUDY PARAMETERS: Bone marrow cytology, cytochemistries, cytogenetics, cell surface marker studies, CSF cytology, chest x-ray, hematologic parameters, liver and kidney function tests, skin tests, serum and CSF MTX levels, IVP, skeletal survey, cultures.

END POINTS: Response/remission rate, duration of remission (complete remission, hematologic remission, CNS remission), survival, toxicities of treatment (especially CNS therapies).

CURRENT STATUS: 200 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Regimen A: PRED - 40 mg/sqm/day po for 28 days; VCR - 1.5 mg/sqm (maximum 2.0 mg)/week iv on days 1, 8, 15, and 22; L-ASP - 10,000 U/sqm iv on days 4, 8, 12, and 15; MTX - 12 mg/sqm (maximum 12 mg) it on days 15 and 29. On attainment of CR, patients are randomized to Arms I and II.

Arm I: MTX - 200 mg/sqm iv push followed by 800 mg/sqm iv over 24 hours; MTX - 12 mg/sqm it within 1 hour of iv push; CF - 30 mg/sqm iv q 6 hours for 2 doses, then 3 mg/sqm po q 12 hours for 3 doses beginning 12 hours after completion of MTX infusion. Begin therapy within 7-10 days from M-1 date, and repeat weekly for a total of 3 courses.

Arm II: 1800 rads cranial irradiation over 2.5 weeks; MTX - 12 mg/sqm (maximum 12 mg) it twice weekly for 5 doses (first dose at end of Induction).

Arm III: Begin 7-10 days after completion of CNS prophylaxis. 6-MP - 50 mg/sqm/day po for 120 weeks; MTX - 25 mg/sqm/week po for 120 weeks; MTX - 200 mg/sqm iv push followed by 800 mg/sqm iv over 24 hours followed by Leucovorin Rescue as in Arm I, q 6 weeks for 12 courses; MTX - 12 mg/sqm (maximum 12 mg) it q 12 weeks over 120 weeks, coinciding with alternate iv courses of MTX during the first 72 weeks. Omit po chemotherapy during the weeks of iv MTX.

Arm IV: Weeks 1-36: 6-MP - 50 mg/sqm/day po; MTX - 25 mg/sqm/week po. Weeks 36-54: CTX - 150 mg/sqm/day po on days 1 through 7; ADR - 35 mg/sqm iv on day 8; repeat q 3 weeks for 6 courses. Weeks 54-72: VM-26 - 150 mg/sqm iv q 2 weeks; ARA-C - 300 mg/sqm iv q 2 weeks. Weeks 72-120: 6-MP - 50 mg/sqm/day po; MTX - 25 mg/sqm/week po. Weeks 1-120: MTX - 12 mg/sqm (maximum 12 mg) it q 12 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

6.0028 PHASE III CHEMOTHERAPY, ENDOCRINE THERAPY & IMMUNOTHERAPY WITH VCR/DNM/PRED, MTX/DM, 6-MP/MTX, AND LEVAMISOLE IN ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) ARG-GATLA-1-LLA-79

OBJECTIVES:

I. Demonstrate whether the decrease of blastic infiltration in bone marrow practiced on day 15 of the induction bears prognostic importance.

II. Demonstrate which is the most effective regimen for the administration of levamisole, daily or intermittent.

PROTOCOL ENTRY CRITERIA: Acute lymphoblastic leukemia patients without previous treatment.

PROTOCOL OUTLINE: Randomized for Immunotherapy only.

Induction: Regimen A: Vincristine, VCR, NSC-67574; Daunomycin, DNM, NSC-82151; Prednisone, PRED, NSC-10023.

Prevention of meningeal infiltration: Regimen B: Intrathecal Methotrexate, MTX, NSC-740; Dexamethasone, DM, NSC-34521.

Maintenance: Regimen C: 6-Mercaptopurine, 6-MP, NSC-755; MTX.

Periodic consolidation: Regimen D: VCR; PRED; MTX; DM.

Immunotherapy:

Arm I: Levamisole, LEV, NSC-177023.

Arm II: Levamisole for 2 consecutive days, weekly.

STRATIFICATION: Age (less/more than 15 years of age); WBC (less/more than 50,000/cumm).

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: VCR - 1.5 mg/sqm iv weekly, days 1, 8, 15, and 22; DNM - 25 mg/sqm iv weekly, days 1, 8, 15, and 22; PRED - 40 mg/sqm po daily.

Regimen B: MTX - 12 mg/sqm/dose, it, 6 doses days 1, 15, and 29 of induction, weekly first month of maintenance.

Regimen C: 6-MP - 300 mg/sqm po twice weekly; MTX - 15 mg/sqm po or im twice weekly.

Regimen D: VCR - 1.5 mg/sqm iv, single dose; PRED - 40 mg/sqm po daily for 7 days; MTX - 2 mg/sqm it; DM - 4 mg/sqm it. Periodic consolidation given in months 1, 2, 3, 4, 5 and 6 and q 3 months thereafter.

Immunotherapy:

Arm I: LEV - 120 mg/sqm po daily.

Arm II: LEV - 120 mg/sqm po 2 consecutive days/week.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: VCR - 1 mg vials; DNM - 20 mg vials; PRED - 40 mg tablets; MTX - 2.5 mg tablets, 50 mg vials; DM - 4 mg vials; 6-MP - 50 mg tablets; LEV - 50 mg tablets.

DATE SUMMARIZED: 02/80

6.0029 INDUCTION, CONSOLIDATION, AND MAINTENANCE MULTI-DRUG COMBINATION CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) EORTC-58791

OBJECTIVES:

I. Investigate whether the percent of CR, the time to CR, and the duration of CR and/or survival can be improved by the rapid injection (at the start of Induction treatment with vincristine/adriamycin/prednisone) of one single, very high dose of cytosine arabinoside.

II. Examine whether a 3-month period of very intensive Consolidation chemotherapy with methotrexate/6-thioguanine/cytosine arabinoside/asparaginase/cyclophosphamide or asparaginase/cyclophosphamide following Induction treatment and preceding a 7-drug plus steroid Maintenance therapy is affecting the duration of CR and the duration of survival.

PROTOCOL ENTRY CRITERIA: Patients with ALL with one or more of the following features: white blood count at least 25,000 WBC/microliter, enlarged mediastinum, T type acute lymphoblastic leukemia (greater than 20 percent blasts making rosettes with SRBC or bounding at least 3 SRBC/blast) or B type acute lymphoblastic leukemia (blasts with surface Ig by direct immuno-fluorescence with specific antisera). Patients must be over 15 and under 65 years of age and must have no hyperuricemia, overt liver failure, jaundice, or high liver enzymes. Patients must have received no prior chemotherapy.

PROTOCOL OUTLINE: Randomized study. Patients are randomized for Induction. During Induction, all patients also receive Regimen A, CNS presymptomatic treatment. Patients in CR following Induction are randomized for Consolidation. All patients still in CR after Consolidation enter Maintenance.

Induction:

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Cytosine arabinoside, ARA-C, NSC-63878; plus Prednisone, PRED, NSC-10023.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. ADR; VCR; plus PRED.

Regimen A: Single-agent Chemotherapy plus Radiotherapy. Methotrexate, MTX, NSC-740; plus Radiotherapy to the brain.

Consolidation:

Arm III: 5-Drug Combination Chemotherapy. MTX; 6-Thioguanine, 6-TG, NSC-752; plus ARA-C; followed by L-Asparaginase, L-ASP, NSC-109229; Cyclophosphamide, CTX, NSC-26271.

Arm IV: 2-Drug Combination Chemotherapy. L-ASP; CTX.

Maintenance: 7-Drug Combination Chemotherapy plus Hormone Therapy. PRED; VCR; ADR; CTX; MTX; BCNU, NSC-409962; Actinomycin-D, ACT-D, NSC-3053; 6-Mercaptopurine, 6-MP, NSC-755.

STRATIFICATION BY: Participating institutions; age: less or more than 15 years; WBC: less than or equal to 25,000 per microliter vs. greater than 25,000 per microliter.

SPECIAL STUDY PARAMETERS: Bone marrow examination, CSF examination, EEG and CAT scan of the brain, blood counts, blood urea, creatinine.

END POINTS: Response/remission rate, percentage of CR, time to CR, length of disease-free survival, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: An entry rate of 80 patients per year should be reached.

DOSAGE SCHEDULE:

Arm I: VCR - 1.4 mg/sqm iv on days 1, 8, 15, 29, and 43; ADR - 30 mg/sqm iv on days 8, 29, and 43; ARA-C - 2,500 mg/sqm iv bolus injection on day 1 or 2 or 3; plus PRED - 60 mg/sqm in 3 equal daily doses po on days 1 to 28, then tapered over days 29 to 43.

Arm II: VCR; ADR; plus PRED as in Arm I.

Regimen A: MTX - 12 mg (children over 3 years of age) or 10 mg (children under 3 years of age) it on days 1, 15, 29, 36, 43, and 50; plus 1800 rads midplane delivered to the skull, base of the skull, and the first 2 cervical vertebrae, in 10 sessions of 180 rads each over a period of 12-14 days during days 43 to 57.

Consolidation:

Arm III: MTX - 15 mg/sqm iv daily on days 1 to 5 of weeks 8, 13, and 18; 6-TG - 240 mg/sqm po daily in 2 equal doses q 12 hours on days 1 to 7 of weeks 10, 15, and 20; ARA-C - 300 mg/sqm iv daily in 2 equal doses q 12 hours on days 1 to 7 of weeks 10, 15, and 20; L-ASP - 1,000 U/kg iv on days 1, 3, and 5 of weeks 21 and 22; CTX - 1,200 mg/sqm (1,000 mg/sqm for patients over 60 years old) iv the day after the last L-ASP dose.

Arm IV: L-ASP - 1,000 U/kg iv on days 1, 3, and 5 of weeks 8 and 9; CTX - 1,200 mg/sqm (1,000 mg/sqm for patients over 60 years old) iv on the day after the last L-ASP dose.

Maintenance: The 70-day sequence of therapy is initiated following Consolidation. PRED - 180 mg/sqm/day po in divided doses on days 1 to 7; VCR - 1 mg/sqm iv on days 1 and 8; ADR - 20 mg/sqm iv on days 15, 16, and 17 of sequences 1, 3, and 5, or BCNU - 80 mg/sqm iv and CTX - 800 mg/sqm/day on day 15 of sequences 2, 4, and 6; 6-MP - 90 mg/sqm po on days 29 to 56; MTX - 10-12 mg it on day 29; MTX - 20 mg/sqm po on days 36, 41, 46, 51, and 56; ACT-D - 1,000 micrograms/sqm iv on day 64. Patients continue therapy, repeating the sequence for 3 years or until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

6.0030 VCR/PRDL, CTX/VCR/ARA-C/MTX/PRDL, L-ASP/VCR/ADR VS VCR/PRDL, 6-MP/L-ASP/MTX/CF, BOTH FOLLOWED BY RADIOTHERAPY AND MAINTENANCE FOR ALL

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PROTOCOL NUMBER(S) UKM-MRC-UKALL-VI

OBJECTIVES:

I. Compare in patients with ALL the regimen employed in UKALL IV with one in which the Consolidation phase includes medium-dose methotrexate in place of the multi-drug Consolidation.

II. Investigate the occurrence of early testicular infiltration and the possibility that the testis is a sanctuary from which re-seeding occurs.

PROTOCOL ENTRY CRITERIA: Patients with ALL with blood leucocytes greater than 20,000/microliter. Lymphoblasts must have T-cell properties. Patients must be at least 14 years of age. Negroes are eligible.

PROTOCOL OUTLINE: Randomized study. Patients are randomized to Arms I and II. Following this treatment, they are rerandomized to Arms III and IV. Male patients are concurrently randomized for testicular irradiation. All patients proceed to Maintenance.

Arm I: Single-agent Chemotherapy plus Hormone Therapy followed by 4-Drug Combination Chemotherapy plus Hormone Therapy followed by 3-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Prednisolone, PRDL, NSC-9900; followed by COAP: Cyclophosphamide, CTX, NSC-26271; VCR; Cytosine arabinoside, ARA-C, NSC-63878; PRDL; plus Methotrexate, MTX, NSC-740; followed by L-asparaginase (Erwinia), L-ASP, NSC-106977; Adriamycin, ADR, NSC-123127; VCR.

Arm II: Single-agent Chemotherapy plus Hormone Therapy followed by 4-Drug Combination Chemotherapy. VCR; PRDL; followed by 6-Mercaptopurine, 6-MP, NSC-755; L-ASP; ARA-C; MTX; Citrovorum Factor, CF, NSC-3590.

Arm III: Radiotherapy plus Single-agent Chemotherapy. Cranial irradiation, 9-fraction schedule; plus 6-MP; (testicular irradiation where applicable).

Arm IV: Radiotherapy plus Single-agent Chemotherapy. Cranial irradiation, 12-fraction schedule; plus 6-MP; (testicular irradiation where applicable).

Maintenance: 4-Drug Combination Chemotherapy plus Hormone Therapy. VCR; MTX; 6-MP; ARA-C; plus PRDL.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Blood counts, bone marrow, lumbar puncture, chest x-ray, urea, urate, transaminases, bilirubin, alkaline phosphatase.

END POINTS: Response/remission rate, duration of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: VCR - 1.5 mg/sqm iv q week for 4 weeks; PRDL - 40 mg/sqm daily tailed in the third week. During weeks 5 and 7 give COAP: CTX - 600 mg/sqm iv on day 1; VCR - 1.5 mg/sqm iv on day 1; ARA-C - 100 mg/sqm on days 1 through 5 (iv on day 1, sc or iv on day 2 through 5); PRDL - 100 mg/sqm po on days 1 through 5. During weeks 3, 5, 7, and 9 give MTX - 10 mg (7.5 mg for patients between 2-3 years of age, 5 mg for one-year-old patients) it. During weeks 9 and 10 give L-ASP - 10,000 U/sqm iv on days 1, 3, 5, and 8; VCR - 1.5 mg/sqm iv on day 1; ADR - 15 mg/sqm iv on day 1

Arm II: VCR - 1.5 mg/sqm iv q week for 4 weeks; PRDL - 40 mg/sqm daily tailed in the fifth week. During weeks 3 and 5 give ARA-C - 50 mg/sqm it; during weeks 4 and 5 give 6-MP - 70 mg/sqm po daily; L-ASP - 10,000 U/sqm iv on days 1, 3, 5, and 8. During weeks 6 to 10 give MTX - 500 mg/sqm iv; one-third dose is given as a rapid injection and the remaining two-thirds is infused over 6 hours, repeated at 10-day intervals for 3 infusions. Eighteen hours after the end of MTX infusion, begin CF - 12 mg/sqm iv; in the succeeding 24 hours, give CF - 18 mg/sqm in 3 divided doses.

Arm III: During weeks 11-13, cranial irradiation - 1800 rads in 9 fractions; plus 6-MP - 35 mg/sqm daily.

Arm IV: During weeks 11-13, cranial irradiation - 2400 rads in 12 fractions; plus 6-MP - 35 mg/sqm daily.

Male patients randomly selected to receive testicular irradiation are given 1200 rads in 6 fractions concurrent with cranial irradiation.

Maintenance: PRDL - 40 mg/sqm po daily (tailing in week 3); VCR - 1.5 mg/sqm on day 1 of weeks 2 and 3; MTX - 15 mg/sqm po daily for 5 days during weeks 4 and 12; 6-MP - 70 mg/sqm po daily during weeks 5-7 and 9-11; ARA-C - 50 mg/sqm sc on day 1 of weeks 6 and 10; MTX - 15 mg/sqm po daily for 4 days during week 8.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

6B. ACUTE MYELOGENOUS AND OTHER ACUTE NON-LYMPHOCYTIC LEUKEMIAS

6.0031 PHASE III REINDUCTION WITH ARA-C/DNM VS CYC/DNM & MAINTENANCE WITH ARA-C/CTX VS CYC/CTX FOR ACUTE NON-ALL/AUL LEUKEMIA

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PROTOCOL NUMBER(S) CCG-243

OBJECTIVES:

I. Determine remission reinduction rate using daunomycin combined with either cytosine arabinoside or cyclocytidine in patients with acute nonlymphocytic leukemia relapsing on previous maintenance regimen of Protocol CCG-241 or CCG-102.

II. Compare duration of bone marrow remission using this combination of agents.

PROTOCOL ENTRY CRITERIA: Patients with acute myelogenous, myelomonocytic, erythro- or monocytic-histiocytic leukemia in relapse from Maintenance of CCG-241 or CCG-102 protocols. Patients must be less than 20 years of age, have an M3 marrow, and are at least 2 weeks past previous chemotherapy in the absence of progressive disease.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I: 2-Drug Combination Chemotherapy. DA: Cytosine arabinoside, ARA-C, NSC-63878; Daunomycin, DNM, NSC-82151.

Arm II: 2-Drug Combination Chemotherapy. DNM; Cyclocytidine, CYC, NSC-145668.

Maintenance: Enter M1 responders from Arm I to Arm III, from Arm II to Arm IV.

Arm III: 2-Drug Combination Chemotherapy. ARA-C; Cyclophosphamide, CTX, NSC-26271.

Arm IV: 2-Drug Combination Chemotherapy. CYC; CTX.

Revised Maintenance (Addenda 1, November 1978, and 2, January 1979).

Arm V: Sequential 2-Drug Combination Chemotherapies. VP-16, NSC-141540; plus CCNU, NSC-79037; or Cyclophosphamide, CTX, NSC-26271; or Cytosine arabinoside, ARA-C, NSC-63878. (ARA-C replaced by CYC, Addendum 3, November 1979.)

STRATIFICATION BY: Participating institutions, prior BCG immunotherapy.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction:

Omit DNM in Arms I and II for patients who have already received 555 mg/sqm.

Arm I: ARA-C - 200 mg/sqm/day iv in 2 divided doses on days 1 through 7; DNM - 30 mg/sqm/day iv on days 1, 2 and 3, not to exceed 550 mg/sqm lifetime dose. Discontinue DNM on cardiac failure or dysfunction. Repeat course on days 14 through 20.

Arm II: CYC - 600 mg/sqm/day sc on days 1 through 7; DNM - as in Arm I. Repeat course on days 14 through 20.

Evaluate patients in Arms I and II on day 28. If marrow is M1, transfer patients from Arm I to Maintenance Arm III, patients from Arm II to Arm IV; if M2, give a third course of chemotherapy on days 28 through 34; if marrow is M3, take patient off study. Re-evaluate patients on day 42; if M1, transfer as above; if M2, but improved over day 28, give a fourth course of chemotherapy on days 42 through 48; if M2 but worsened since day 28 or M3, remove patient from study. Re-evaluate patients on day 56; if M1, transfer as above, if M2 or M3 remove patients from study. Remove from study if disease status has changed from C to D, or deterioration has occurred within status D with no improvement in marrow.

Maintenance:

Arm III: ARA-C - 200 mg/sqm/day iv or im in 2 divided doses on days 1 through 7; CTX - 75 mg/sqm/day po on days 1 through 21. Repeat course q 28 days.

Arm IV: CYC - 600 mg/sqm/day sc on days 1 through 7; CTX - as in Arm III. Repeat course q 28 days.

Revised Maintenance:

Arm V: Courses are given q 3 weeks. Course 1. VP-16 - 150 mg/sqm iv (reduced to 100 mg/sqm, iv drip over one hour, Addendum 3, November 1979) on days 1 through 5; CCNU - 100 mg/sqm po on day 1. Course 2. VP-16 - as above; CTX - 300 mg/sqm iv on day 1. Course 3. VP-16 - as above; ARA-C - 150 mg/sqm/day iv given in 2 divided doses q 12 hours on days 1 through 5. (CYC - 400 mg/sqm/day has replaced ARA-C, Addendum 3, November 1979.)

Repeat sequence q 9 weeks.

Dosage modifications for toxicity and intrathecal methotrexate therapy for CNS disease are given.

DOSAGE FORMS: ARA-C - 100 and 500 mg vials; DNM - 20 mg vials; CYC - 100 and 500 mg vials; CTX - 25 and 50 mg tablets.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00560279

6.0032 PHASE III COMBINATION CHEMOTHERAPY (CYCLIC VS CONTINUOUS) VS BONE MARROW TRANSPLANTATION IN PEDIATRIC ACUTE NON-LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) CCG-251

OBJECTIVES:

I. Improve remission duration and survival in children with previously untreated acute non-lymphocytic leukemia using: cyclophosphamide (CTX) and total body irradiation followed by bone marrow transplantation (BMT) with compatible donor marrow for children who achieved complete remission with induction therapy.

II. Compare two intensive maintenance regimens: (a) continuous 6-thioguanine (6-TG) with monthly courses of CTX, vincristine (VCR), 5-azacytidine (5-AZA) and cytosine arabinoside (ARA-C), and (b) repeated cycles of 6-TG and ARA-C; adriamycin (ADR) and ARA-C; prednisolone (PRDL), VCR, methotrexate (MTX) and 6-mercaptopurine (6-MP); 5-AZA and ADR; BCNU and CTX.

III. Evaluate the induction capabilities of ADR plus ARA-C.

IV. Evaluate the prognostic significance of chromosomal abnormalities in leukemic cell lines.

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age with previously untreated acute non-lymphocytic leukemia.

PROTOCOL OUTLINE: Randomized study.

Enter all patients to Induction Regimen. Patients with a compatible donor who achieve bone marrow remission and who elect transplantation receive preparative Chemotherapy and Radiotherapy followed by allogenic bone marrow transplantation (BMT). Patients ineligible for marrow graft receive CNS Intensification Radiotherapy and Chemotherapy, then are randomized into Maintenance Arm I or Arm II.

Induction:

2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cytosine arabinoside, ARA-C, NSC-63878 given iv.

Maintenance; Patients receive maximum three years of Maintenance Therapy.

Regimen A: Marrow Transplantation: Patients with a compatible donor who achieve M-1 or M-2A bone marrow remission and who elect marrow transplantation, receive Cyclophosphamide, CTX, NSC-26271 followed by total body irradiation, followed by allogenic BMT. Methotrexate, MTX, NSC-740 is administered after BMT for graft vs. host disease prevention.

Regimen B: Patients not receiving BMT receive CNS Intensification Cranial Radiotherapy with Cobalt-60, 4 or 6 MeV x-rays, or higher photon energies, plus concurrent cycles of Combination Chemotherapy of CAT (ARA-C/6-TG) 6-Thioguanine, 6-TG, NSC-752 plus MTX-intrathecal (MTX-IT).

Arm I: Patients randomized from Regimen B, continuous 6-Drug Combination Chemotherapy repeated every 28 days. CAT; Vincristine, VCR, NSC-67574; 5-Azacytidine, 5-AZA, NSC-102816; CTX; MTX-IT.

Arm II: Patients randomized from Regimen B, cyclic Combination Chemotherapy repeat cycles A through E every 112 days, MTX; CAT; CVA (CTX/VCR/ADR); Prednisolone, PRDL, NSC-9151; 6-Mercaptopurine, 6-MP, NSC-755; 5-AZA; BCNU, NSC-409962.

STRATIFICATION BY: Initial wbc, age, participating institutions.

SPECIAL STUDY PARAMETERS: Initial and continuous evaluation of: BM cytological criteria; chromosome analysis; CSF: cell count, cytology, protein, sugar and culture; kidney and liver function tests: BUN, uric acid, SGOT, SGPT, alkaline phosphatase. Patients eligible for BMT undergo immunological donor compatibility typing (MLC and HLA), including their parents and siblings.

END POINTS: Response/remission rate, duration of remission, relapse rate, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: At least 176 patients will be entered in 3.5 years.

DOSAGE SCHEDULE:

Induction:

ADR - 30 mg/sqm days 1-3 and 15-17; ARA-C - 100 mg/sqm days 1-7 and 15-21 by continuous iv infusion. If on day 14 marrow is hypocellular, normocellular with fewer than 15 percent blasts, give ADR on days 15 and 16 and ARA-C on days 15-19. Patients with M-2 BM on day 29 continue induction: ADR days 29-31 and ARA-C days 29-35. On day 43, M-2A patients continue induction: ADR days 43-45; ARA-C days 43-49.

Bone Marrow Transplantation: (BMT) Patients who achieve remission criteria of M-1 on days 29 or 43 or 57 (M-1 or M-2A) of induction undergoing BMT receive preparative CTX - 60 mg/kg days 1 and 2, followed by total body irradiation of 1000 rad day 6, followed by allogenic BMT day 7. Transplantation will utilize 3-5 x 10 to the eighth nucleated marrow cells per kg. After BMT, patients receive MTX: 15 mg/sqm iv on day 1 and 10 mg/sqm iv on days 3, 6, 11, 18 and q 7 days for 100 days.

Arm I and II: Preventive CNS Radiation Therapy: Cranial exposure to 180 rads per day in 10 fractions over 12-14 days, total 1800 rads.

Maintenance:

Patients begin Maintenance when AGC is greater than 750 and platelet count greater than 100,000/cmm.

Arm I and II: Concurrent with Radiation Therapy: 6-TG - 60 mg/sqm po days 1-4, 8-11, 15-18; ARA-C - 50 mg/sqm sc days 5, 12, 19; MTX-IT dosage (6-12 mg/sqm) graduated by age, less than 1 year to over 3 years, days 1, 8, 15.

Arm I: Continuous-repeated every 28 days. 6-TG - 75 mg/sqm po days 1-28; ARA-C - 75 mg/sqm iv days 1-4; CTX - 75 mg/sqm iv days 1-4; VCR - 1.5 mg/sqm iv day 1; AZA-5 - 100 mg/sqm iv days 1-4; MTX-IT dose graduated by age (6-12 mg/sqm) administered on day 1 of the first 4 courses of treatment.

Arm II: Cyclic-repeat Cycles A-E every 112 days. MTX-IT dose graduated according to age (6-12 mg/sqm) day 1 of Cycles A-D of first 112-day course.

Cycle A: ADR - 30 mg/sqm iv day 1; ARA-C - 100 mg/sqm continuous iv infusion days 1, 2, 3, 4, 5. Discontinue ADR when a cumulative dose of 480 mg/sqm is reached.

Cycle B: PRDL - 1 g/sqm iv days 22, 23, 24, 25; VCR - 2 mg/sqm iv day 22; MTX - 7.5 mg/sqm iv days 22, 23, 24, 25; 6-MP - 500 mg/sqm po days 22, 23, 24, 25.

Cycle C: 5-AZA - 150 mg/sqm iv continuous infusion days 43, 44, 45, 46, 47; ADR - 30 mg/sqm iv day 43.

Cycle D: BCNU - 200 mg/sqm iv day 71; CTX - 1000 mg/sqm iv day 71.

Cycle E: 6-TG - 60 mg/sqm po days 92-95, 99-102, 106-109; ARA-C - 50 mg/sqm days 96, 103, 110.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; MTX - 5 and 50 mg vials; 6-MP - 50 mg tablets; CTX - 100, 200 and 500 mg vials; ADR - 10 mg vials; ARA-C - 100 and 500 mg vials; 5-AZA - 50 mg vials; 6-TG - 40 mg tablets; BCNU - 100 mg vials; PDRL - 20 mg/ml.

DATE SUMMARIZED: 02/80

6.0033 PHASE III INDUCTION WITH DNM/ARA-C/TG AND MAINTENANCE WITH DNM/ARA-C/TG/VCR/PRED FOR ACUTE MYELOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) CLB-7921

OBJECTIVES:

I. Compare effect of induction combination chemotherapy with daunomycin(DNM)/7 days cytosine arabinoside (ARA-C) vs. DNM/10 days ARA-C vs. DNM/ARA-C/6-thioguanine (TG) for acute myelocytic leukemia.

II. Determine effect of co-trimoxazole administration during Induction.

III. Compare effect of Maintenance combination chemotherapy with DNM/ARA-C/TG/VCR/PRED for 2 cycles vs. until relapse.

PROTOCOL ENTRY CRITERIA: Patients with chemically and histologically confirmed FAB Stage M1 through M6, acute myelocytic leukemia. Patients must have adequate liver function and normal kidney function and must not have prior cytotoxic therapy or extensive radiation therapy.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arm I, II, and III, then rerandomize to treatment with or without Co-trimoxazole.

Induction:

Arm I: 2-Drug Combination Chemotherapy. Daunomycin, DNM, NSC-82151; Cytosine arabinoside, ARA-C, NSC-63878.

Arm II: 3-Drug Combination Chemotherapy. DNM; ARA-C; 6-Thioguanine, TG, NSC-752.

Arm III: 2-Drug Combination Chemotherapy. DNM/ARA-C.

Maintenance:

Regimen A: 4-Drug Combination Chemotherapy plus Hormone Therapy. ARA-C; TG; DNM; Vincristine, VCR, NSC-67574; plus Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Measurement of liver, spleen, and lymph nodes; CBC; bone marrow aspirate and biopsy; stool occult blood; liver and kidney function; cerebrospinal fluid examination; skin tests for recall antigens.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: 600 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: DNM - 45 mg/sqm iv rapid infusion on days 1, 2, and 3; ARA-C - 100 mg/sqm/ day iv continuous infusion on days 1 through 7.

Arm II: DNM; ARA-C as in Arm I; TG - 100 mg/sqm po twice a day on days 1 through 7.

Arm III: DNM; ARA-C as in Arm I except ARA-C on days 1 through 10.

Co-trimoxazole - 2 regular strength tablets po twice a day from day before initiation of Induction Therapy until remission or removal from study.

Seven days after completion of first Induction course, perform bone marrow aspirate and biopsy. If marrow cellularity is normal with 5 percent or fewer leukemia cells (M1 marrow), enter patient to Maintenance. If marrow is aplastic or hypocellular (less than 1+) and M1, wait 1 week and repeat marrow aspirate and biopsy. When marrow cellularity returns to normal and M1, enter patient to Maintenance. If marrow cellularity is 1+ or greater and marrow contains more than 5 percent leukemic cells, give second course of Induction restricting ARA-C and TG to 5 days and DNM to 2 days, and determine eligibility for entering Maintenance as above. If cellularity of marrow is 0 and regeneration is delayed more than 21 days after completion of second Induction course and if marrow is at least M2, enter patient to Maintenance. If marrow does not achieve M2 after recovery from second course of Induction, remove patient from study.

Maintenance: Patients must have skin test for recall antigens and granulocytes at least 2000/cumm and platelets at least 100,000/cumm before being entered.

Regimen A: ARA-C - 100 mg/sqm sc twice a day on days 1 through 5 of months 1 through four; TG - 100 mg/sqm po twice a day on days 1 through 5 of month 1; DNM - 45 mg/sqm (maximum cumulative dose 500 mg/sqm) iv on days 1 and 2 of month 3; VCR - 2 mg/sqm (maximum dose 2 mg) iv on day 1 of months 2 and 4; PRED - 40 mg/sqm (maximum dose 100 mg) po in 3 divided doses on days 1 through 5 of months 2 and 4. Repeat 4-month cycle once more. Then randomize patients to discontinue or continue Maintenance if marrow is M1 or M0. If marrow is M2, reinduce. Adjust DNM dosage for patients randomized to continuing Maintenance as follows: remission after 1 course of Induction therapy and full doses of DNM during Maintenance therapy - discontinue DNM after fourth cycle; remission after 2 courses of Induction therapy and full dose of DNM during Maintenance therapy - discontinue DNM after third cycle; substitute TG - 100 mg/sqm po twice a day on same days as ARA-C. When patients relapse after randomization to 2-cycle or continuing Maintenance, reinduce using original Induction therapy. Reinduction is limited by the maximum allowable cumulative dose of DNM (500 mg/sqm).

Dosage modifications for toxicity are given.

DOSAGE FORMS: ARA-C - 100 and 500 mg vials; DNM - 20 mg vials; TG - 40 mg scored tablets; VCR - 1 and 5 mg vials; PRED - 5, 10, and 20 mg tablets; Co-trimoxazole (Septra, Bactrim) - single and double strength tablets.

DATE SUMMARIZED: 02/80

6.0034 COMBINATION CHEMOTHERAPY WITH DNM/ARA-C/6-TG WITH OR WITHOUT CONSOLIDATION FOR ACUTE NON-LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) EST-1479

OBJECTIVES:

I. Confirm the significant decrease in the median time of induction suggested by the Sloan-Kettering data and EST pilot study when using daunomycin (DNM)/cytosine arabinoside (ARA-C)/thioguanine (6-TG) for acute non-lymphocytic leukemia.

II. Determine the benefit of intensive consolidation therapy upon complete response duration.

III. Assess the toxicity of intensive consolidation.

PROTOCOL ENTRY CRITERIA: Patients with morphologically proven acute disease of any of the following types: myeloblastic, promyelocytic, myelomonocytic, or monocytic leukemia; erythroleukemia. Patients must be between 15 and 70 years old and must have no prior chemo- or radiotherapy. Patients must have a performance status of 0, 1 or 2 and adequate cardiac, hepatic and renal status.

PROTOCOL OUTLINE: Randomized study.

Enter all patients to Induction; randomize complete responders to Consolidation or Maintenance.

Induction: 3-Drug Combination Chemotherapy. Daunomycin, DNM, NSC-82151; Cytosine arabinoside, ARA-C, NSC-63878; Thioguanine, 6-TG, NSC-752.

Consolidation: 3-Drug Combination Chemotherapy. DNM; ARA-C; 6-TG.

Maintenance: 2-Drug Combination Chemotherapy. ARA-C; 6-TG.

STRATIFICATION BY: Participating institutions; age: 15 to 35 vs. 36 to 59 vs. 60 or over; number of induction courses before complete response: 1 vs. 2.

SPECIAL STUDY PARAMETERS: Lumbar puncture.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, relapse rate, duration of response.

CURRENT STATUS: Approximately 250 patients to be entered in 2.5 years.

DOSAGE SCHEDULE:

Induction: DNM - 60 mg/sqm iv on days 1 through 3; ARA-C - 25 mg/sqm iv on day 1, followed by 200 mg/sqm iv infusion on days 1 through 5; 6-TG - 200 mg/sqm po on days 1 through 5.

Evaluate patients after 7 days. Randomize patients with complete response to Consolidation or Induction. Repeat Induction for 1 additional course if response is not complete, then randomize complete responders. Remove all others from study.

Consolidation: Begin 1 to 4 weeks after last Induction. DNM - 45 mg/sqm iv on days 1 and 2; ARA-C - 200 mg/sqm iv infusion on days 1 through 5; 6-TG as in Induction. Repeat once after a 1-month rest. Enter patients still in remission to Maintenance.

Maintenance: 6-TG - 80 mg/sqm po on days 1 through 4; ARA-C - 60 mg/sqm sc on day 5. Repeat q 7 days for 22 months or until relapse. Follow for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ARA-C - 100 and 500 mg vials; DNM - 20 mg vials; 6-TG - 40 mg tablets.

DATE SUMMARIZED: 02/80

6.0035 PHASE II CHEMOTHERAPY WITH VP-16 VS AMSA FOR PATIENTS WITH ACUTE NONLYMPHOCYTIC LEUKEMIA IN RELAPSE

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PROTOCOL NUMBER(S) EST-4479

OBJECTIVES:

I. Determine effects of single-agent chemotherapy with VP-16213 (VP-16) vs. AMSA for patients with acute nonlymphocytic leukemia who have failed on prior chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients at least 15 years of age with morphologically proven acute nonlymphocytic leukemia (granulocytic, myelomonocytic, monocytic, promyelocytic, and erythro) who have failed or relapsed on prior chemotherapy (as in EST-2476 or EST-1479). Patients must have: reached nadir counts and stabilized for 3 to 5 days following prior chemotherapy, performance status of at least 2, and adequate kidney and liver function.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. VP-16, NSC-141540.

Arm II: Single-agent Chemotherapy. AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions; performance status: 0 or 1 vs. 2; age: less than 30 vs. 30-59 vs. 60 or over.

SPECIAL STUDY PARAMETERS: CBC; liver and kidney function; SMA-6; node, liver and spleen measurement; marrow aspirate smear.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 40 patients will be entered in each Arm.

DOSAGE SCHEDULE:

Arm I: VP-16 - 100 mg/sqm iv on days 1 through 5. Retreat with 125 mg/sqm iv on days 1 through 5 for patients who show no significant toxicity after 21 days and no complete or partial remission. Maintain until relapse patients in complete or partial remission: 100 mg/sqm on days 1 through 3 q 3 weeks.

Arm II: AMSA - 200 mg/sqm iv over 30 minutes in 250 ml D5W on days 1 through 5. Retreat with a second course patients who show no significant toxicity after 21 days and no complete or partial remission. Maintain until relapse patients in partial or complete remission: 40 mg/sqm on days 1 through 3 q 3 weeks.

Remove from study patients in progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VP-16 - 100 mg ampules; detailed dosage forms for AMSA are given.

DATE SUMMARIZED: 02/80

6.0036 COMBINATION CHEMOTHERAPY WITH ARA-C/TG OR ARA-C/TG/DNM FOR ADULT ACUTE NONLYMPHOCYTIC LEUKEMIAS

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PROTOCOL NUMBER(S) NCOG-P-9L81

OBJECTIVES:

I. Determine the complete remission rate of patients treated initially with cytosine arabinoside (ARA-C)/thioguanine (TG).

II. Determine the complete remission rate of patients who fail on ARA-C/TG and who later receive daunomycin (DNM).

III. Assess the duration of unmaintained remission in those patients who enter a complete remission with ARA-C/TG and subsequently receive 3 Consolidation courses as opposed to those patients who fail Induction with ARA-C/TG and are subsequently put into remission with DNM/ARA-C/TG followed by 3 Consolidation courses.

PROTOCOL ENTRY CRITERIA: Patients with the following acute nonlymphocytic leukemias: myelogenous, promyelocytic, myelomonocytic, monocytic, or erythroleukemia. Patients must not have had prior therapy with the study agents, and they must have adequate cardiac status and controlled serum uric acid levels. Patients with controlled symptomology will be eligible only upon deterioration.

PROTOCOL OUTLINE: Nonrandomized study. Cross over patients with inadequate response in Regimen A to Regimen B.

Regimen A: 2-Drug Combination Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878; Thioguanine, TG, NSC-752. Enter patients with M-1 marrow to Consolidation. Enter all other patients to Regimen B.

Regimen B: 3-Drug Combination Chemotherapy. ARA-C, TG; Daunomycin, DNM, NSC-82151. Enter patients with M-1 marrow to Consolidation.

Consolidation. 2-Drug Combination Chemotherapy. ARA-C, TG.

Maintenance. 2-Drug Combination Chemotherapy. ARA-C, TG.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Labeling index with radioactively labeled thymidine.

END POINTS: Response/remission rate, duration of response, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: At least 40 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: ARA-C - 100 mg/sqm iv q 12 hours on days 1 through 5; TG - 80 mg/sqm po q 12 hours on days 1 through 5. Enter patients to Consolidation if marrow is M-1 on day 20. If cellularity is 50% or greater than initial aspirate, continue ARA-C/TG for 3 or 6 days. After day 12, if M-1 is still not achieved, enter patients to Regimen B. If cellularity is 50% or less after day 20, but increases above 50%, repeat Regimen A for up to 3 courses.

Regimen B: ARA-C - 100 mg/sqm iv q 12 hours on days 1 through 5; TG - 80 mg/sqm po q 12 hours on days 1 through 5; DNM - 45 mg/sqm (maximum cumulative dose 550 mg/sqm) iv on days 1 through 3.

Enter patients to Consolidation after 3 to 5 weeks of rest if marrow is M-1. Repeat course once for all other patients, then remove from study if not M-1.

Consolidation. ARA-C - 100 mg/sqm iv q 12 hours on days 1 through 5; TG - 80 mg/sqm po q 12 hours on days 1 through 5. Repeat course q 21 to 28 days for 3 courses provided M-1 or M-2 marrow is maintained.

Maintenance: Follow up patients q month. On relapse, enter patients to Regimen A or Regimen B, depending on prior response. If complete response lasted less than 3 months, give ARA-C - 100 mg sc q 12 hours on days 1 through 5; TG - 80 mg po q 12 hours on days 1 through 5. Repeat course q 4 weeks.

Dosage modification for toxicity are not given.

DOSAGE FORMS: ARA-C - 100 and 500 mg vials; TG - 40 mg tablets; DNM - 20 mg ampules.

DATE SUMMARIZED: 02/79

6.0037 CHEMOTHERAPY WITH AZC/TG FOR REFRACTORY ADULT ACUTE NONLYMPHOCYTIC LEUKEMIA (ANLL)

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PROTOCOL NUMBER(S) NCOG-9L62

OBJECTIVES:

I. Determine effect of combination chemotherapy with 5-azacytidine (AZC) and 6-thioguanine (TG) in adult patients with acute nonlymphocytic leukemia resistant to cytosine arabinoside (ARA-C) and anthracyclines or ineligible for further anthracycline therapy.

PROTOCOL ENTRY CRITERIA: Patients over 16 years of age with acute nonlymphocytic leukemia (acute granulocytic with minimal or significant differentiation, hypergranular acute promyelocytic, acute myelomonocytic, acute monocytic or erytholeukemia) who are not eligible for further treatment with anthracyclines or are refractory to anthracyclines and ARA-C.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. 5-Azacytidine, AZC, NSC-102816; 6-Thioguanine, TG, NSC-752.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: PT, PTT, fibrinogen, liver and kidney function, spleen size measurements, electrolytes.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, length of survival, survival rate.

CURRENT STATUS: 50 patients will be entered in 15 months.

DOSAGE SCHEDULE:

Induction:

Course 1: AZC - 150 mg/sqm/day iv continuous infusion for 5 days; TG - 80 mg/sqm po q 12 hours for 5 days.

Course 2: Administer only if bone marrow aspirate indicates patient is not in complete remission 9 to 16 days after course 1. AZC - 200 mg/sqm/day iv continuous infusion for 5 days; TG - as in course 1.

Course 3: Administer only if bone marrow aspirate indicates patient is not in complete remission 9 to 16 days after course 2 therapy. AZC - as in course 2; TG - 120 mg/sqm q 12 hours for 7 days.

Remove from study patients who have M-3B or M-4 marrow 9 to 16 days after completing therapy. Remove from study patients who do not have M-1 marrow by 9 to 30 days after completing therapy, and patients who relapse and do not respond to 3 Induction regimens. Follow patients until resistance to therapy is demonstrated.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZC - 100 mg vials; TG - 40 mg tablets.

DATE SUMMARIZED: 10/79

6.0038 PHASE II CHEMOTHERAPY WITH AMSA FOR ACUTE NONLYMPHOCYTIC LEUKEMIAS REFRACTORY TO STANDARD THERAPY

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PROTOCOL NUMBER(S) NCOG-9L83

OBJECTIVES:

I. Determine the efficacy of AMSA for patients with nonlymphocytic leukemia who are resistant to cystosine arabinoside.

II. Determine the effect on this treatment of prior therapy with daunomycin and/or adriamycin, Karnofsky performance status, histologic type, marrow status, and marrow cellularity.

PROTOCOL ENTRY CRITERIA: Patients not under 16 years old with acute nonlymphocytic leukemia (myelogenous, onocytic, myelomonocytic, promyelocytic or erythroleukemia) or smouldering or subacute disease which has progressed. Patients must have adequate serum uric acid levels and renal and hepatic function and must be refractory to standard therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction and Maintenance: Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: Participating institutions, previous therapy, Karnofsky performance status, histologic type, marrow status.

SPECIAL STUDY PARAMETERS: Bone marrow aspiration.

END POINTS: Response/remission rate, duration of response, survival rate, toxicity/morbidity of treatment, survival time, disease-free interval.

CURRENT STATUS: 90 to 100 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Induction: AMSA - 100 mg/sqm iv on days 1 through 5. Repeat course q 3 weeks until M-1 marrow is reached or therapy shows no improvement after 2 successive cycles. Cycle may start before 3 weeks are up if toxicity has abated. Patients may be removed from study if M-4 marrow persists for two or more cycles. Patients with M-1 marrow proceed to Maintenance.

Maintenance: AMSA - 100 mg/sqm iv on days 1 through 3 q 3 weeks until resistance to therapy is demonstrated. Follow-up all patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg vials.

DATE SUMMARIZED: 11/79

6.0039 PHASE II PILOT CHEMOTHERAPY WITH VINBLASTINE FOR REFRACTORY ACUTE MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) SEG-AML-P30

OBJECTIVES:

I. Determine the activity of vinblastine (VBL) in the treatment of refractory acute myelogenous leukemia.

PROTOCOL ENTRY CRITERIA: Patients with acute myelogenous leukemia refractory to standard therapy. Patients must have a performance status of 40 or better, a minimum life expectancy of 1 month, and adequate hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: Single-agent Chemotherapy. Vinblastine, VBL, NSC-49842.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: None

END POINTS: Response/remission rate.

CURRENT STATUS: 25 patients will be entered

Induction: VBL - 0.15 mg/kg iv on days 1 through 3. Repeqt q 10 days until an M-1 marrow is obtained and as long as marrow blast cells are decreasing. Follow all patients until relapse. Examine bone marrow of patients in complete remission q month for 3 months, then q 2 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: VBL - 5 mg vials.

DATE SUMMARIZED: 11/78

6.0040 PHASE III INDUCTION WITH CYTOSINE ARABINOSIDE/DAUNOMYCIN WITH OR WITHOUT LITHIUM CARBONATE FOR ACUTE MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) SEG-A07

OBJECTIVES:

I. Evaluate the efficacy of lithium carbonate in limiting the degree and duration of neutropenia as well as the number of infections during induction therapy of acute myelogenous leukemia.

II. Confirm the effectiveness of remission induction with daunomycin and cytosine arabinoside. This protocol is designed in such a manner that patients achieving a favorable response are eligible for the consolidation and maintenance phases of SEG-77AML0103.

PROTOCOL ENTRY CRITERIA: Patients over 15 years old with morphologically and histochemically confirmed acute leukemia (myeloblastic, myelomonocytic, monocytic, promyelocytic or erythrocytic).

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. AD: Cytosine arabinoside, ARA-C, NSC-63878; Daunomycin, DNM, NSC-82151.

Arm II: 2-Drug Combination Chemotherapy plus Supportive Therapy. ARA-C; DNM; plus Lithium carbonate, NSC-16895.

STRATIFICATION BY: Participating institutions; granulocyte count: greater than 1000/cumm vs. less than 1000/cumm; age: over vs. under 60 years.

SPECIAL STUDY PARAMETERS: EKG, skin tests, tests of hepatic and renal function, marrow biopsy, marrow colony forming units, urine colony stimulating activity.

END POINTS: Response/remission rate, morbidity/toxicity of treatment, duration of neutropenia, infection rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: AD: ARA-C - 100 mg/sqm iv on days 1 through 7; DNM - 45 mg/sqm iv on days 1 through 3. Repeat course q 21 days until leukocyte count falls below 1000/cumm or abnormal cells disappear from blood.

Arm II: AD as in Arm I, plus Lithium carbonate - 900 mg/day po in 3 doses with meals on days 3 through 42. If after one or more courses of Induction an M-1 marrow is achieved, or if after 2 courses, an M-2 marrow is achieved, randomize the patient to Consolidation as per SEG-AML0103.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ARA-C - 100 and 500 mg vials; DNM - 20 mg vials; Lithium carbonate - 300 mg tablets.

DATE SUMMARIZED: 09/78

6.0041 PHASE III THERAPY WITH DNM, ARA-C, AZC, BETA-TGDR, TG & BCG FOR INDUCTION, CONSOLIDATION & MAINTENANCE OF ACUTE MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) SEG-77AML0103; SEG-77AML318

I. Confirm the effectiveness of remission induction with daunomycin (DNM)/cytosine arabinoside (ARA-C) for acute myelogenous leukemia.

II. Compare the efficacy of 5-azacytidine (AZC) vs. AZC/betadeoxythioguanosine vs. thioguanine/ARA-C/DNM for consolidation.

III. Compare the efficacy of DNM/ARA-C vs. BCG vs. DNM/ARA-C/BCG for maintenance.

PROTOCOL ENTRY CRITERIA: Patients with histochemical diagnosis of any acute myelogenous leukemia who are untreated and at least 15 years old.

PROTOCOL OUTLINE: Enter all patients to Induction. Responders are randomized for Consolidation. Patients in complete remission following Consolidation are randomized for Maintenance.

Induction: 2-Drug Combination Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878; Daunomycin, DNM, NSC-82151.

Consolidation: Arms I, II, and III.

Arm I: Single-agent Chemotherapy. Azacytidine, AZC, NSC-102816.

Arm II: 2-Drug Combination Chemotherapy. AZC; Betadeoxythioguanosine, Beta-TGdR, NSC-71261.

Arm III: 3-Drug Combination Chemotherapy. Thioguanine, TG, NSC-752; ARA-C; DNM.

Maintenance: Arms IV, V, and VI.

Arm IV: 2-Drug Combination Chemotherapy. DNM; ARA-C.

Arm V: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm VI: 2-Drug Combination Chemotherapy plus Immunotherapy. DNM; ARA-C plus BCG.

STRATIFICATION BY: Participating institutions, age, initial performance status, initial platelet count, initial BUN.

SPECIAL STUDY PARAMETERS: Skin tests for recall antigens, bone marrow tests, lumbar puncture, liver and kidney function tests.

END POINTS: Response/remission rate, duration of remission, length of survival.

CURRENT STATUS: About 532 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Induction: ARA-C - 100 mg/sqm/day iv continuous infusion on days 1 through 7; DNM - 45 mg/sqm/day iv rapid injection on days 1, 2 and 3. Repeat course q 21 days. Randomize patients achieving complete (M1 marrow) or partial (M2 marrow) remission after 2 courses to consolidation therapy.

Consolidation:

Arm I: AZC - 150 mg/sqm/day iv continuous infusion for 5 days.

Arm II: AZC - as in Arm I; Beta-TGdR - 300 mg/sqm/day iv push for 5 days.

Arm III: TG - 100 mg/sqm po q 12 hours for 10 doses; ARA-C - 100 mg/sqm iv push q 12 hours for 10 doses; DNM - 10 mg/sqm iv push q 24 hours for 5 doses.

Repeat all arms q 21 days. If patient is still in, or partial responder achieves, complete remission after 3 courses, randomize to Maintenance therapy.

Maintenance:

Arm IV: Allow 12 weeks after randomization without therapy. DNM -as in Induction on days 1 and 2 of week 13; ARA-C - as in Induction on days 1 through 5 of week 13. Repeat every 13 weeks for 1 year.

Arm V: BCG - vaccinate each extremity twice each week with twice 3 drops/disc/site q week for 4 weeks. Skin test 2 weeks later. If patient converts to positive or is more positive than at entry, repeat vaccination q 4 weeks for 1 year. If patient does not show such a change but is still in remission, continue vaccination twice each week for 4 weeks before proceeding with vaccination q 4 weeks for 1 year.

Arm VI: BCG - as in Arm V; DNM - as in Arm IV; ARA-C - as in Arm IV.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ARA-C - 100 and 500 mg vials; DNM - 20 mg vials; TG - 40 mg tablets; AZC - 100 mg vials; Beta-TGdR - 200 mg vials; BCG - ampules.

PATIENT ACCRUAL: 00560678

6.0042 PHASE II-PILOT CHEMOTHERAPY WITH ANGUIDINE FOR ACUTE NONLYMPHOCYTIC LEUKEMIA REFRACTORY TO STANDARD THERAPY

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PROTOCOL NUMBER(S) SWOG-8063

OBJECTIVES:

I. Determine the efficacy of anguidine for inducing a response in adults with acute nonlymphocytic leukemia refractory to standard forms of therapy.

II. Assess the toxicity of this agent.

PROTOCOL ENTRY CRITERIA: Adult patients with acute nonlymphocytic leukemia resistant to standard therapies who are not eligible for a higher priority protocol. Patients must be over 21 years of age and have an M-3 marrow and a life expectancy of at least 4 weeks. Patients should have recovered from prior significant drug toxicity. Liver and kidney function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Induction. Single-agent Chemotherapy. Anguidine, ANG, NSC-141537; Allopurinol, NSC-1390.

Regimen B: Maintenance. Single-agent Chemotherapy. ANG; Allopurinol.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Performance status, complete neurologic examination, bone marrow aspirations, hemogram, kidney and liver function tests.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 45 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Induction. ANG - 6 mg/sqm/day iv infusion over 8 hours on days 1 through 5. Patients showing marrow in CR on day 14 proceed directly with Regimen B. Those with 14-day marrow showing PR or stable disease repeat Induction. Those with no response or increasing disease may be given a second Induction course or may go off study. A repeat bone marrow is done on day 28. Those with CR proceed with Maintenance; those with partial response may proceed with Regimen B or go off study.

Regimen B: Maintenance. ANG - 5 mg/sqm iv by 4-hour iv infusion. Repeat q 28 days until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ANG - 5 mg vials.

DATE SUMMARIZED: 08/80

6.0043 ARA-C/TG MAINTENANCE WITH/WITHOUT SPLENECTOMY OR ALLOGENEIC MYELOBLASTS AFTER DNM/ARA-C INDUCTION FOR ACUTE NONLYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) BCRP-7802

OBJECTIVES:

I. Compare remission duration and survival of patients with acute nonlymphocytic leukemia treated with cytosine arabinoside (ARA-C)/daunomycin induction therapy and maintenance consisting of ARA-C/thioguanine alone or with either neuraminidase-treated allogeneic myeloblasts or splenectomy.

II. Study the effects of chemotherapy and immunotherapy on blood and marrow CSF and CFU-C.

III. Determine the differential effectiveness of microbial suppres-

PROTOCOL ENTRY CRITERIA: Previously untreated patients with acute nonlymphocytic leukemia as diagnosed morphologically and histochemically by Wright-Giemsa, Sudan black, PAS, and esterase marrow stains; patients must also be terminal-transferase negative. Patients may not have been treated previously for another malignancy except by surgery.

PROTOCOL OUTLINE: Randomized study. Enter all patients on Regimen A. Following CR, randomize patients to Arms I, II, or III. At the same time, randomize patients in each arm to receive oral antibiotics plus laminar air flow treatment or oral antibiotics alone.

Induction.

Regimen A: 2-Drug Combination Chemotherapy. Daunomycin, DNM, NSC-82151; Cytosine arabinoside, ARA-C, NSC-63878.

Maintenance.

Arm I: 2-Drug Combination Chemotherapy. ARA-C; 6-Thioguanine, TG, NSC-752.

Arm II: 2-Drug Combination Chemotherapy plus Immunotherapy. ARA-C; TG; Neuraminidase-treated allogeneic blast cells.

Arm III: 2-Drug Combination Chemotherapy plus Surgery. ARA-C; TG; Splenectomy.

STRATIFICATION BY: Surgical risk (good vs. poor).

SPECIAL STUDY PARAMETERS: HLA typing, hematologic parameters, SMA-12, clotting studies, creatinine, EKG, chest x-ray, bone marrow biopsy, CSF examination, skin tests.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: DNM - 45 mg/sqm by slow iv push on days 1, 2, and 3; ARA-C - 100 mg/sqm/day by continuous iv infusion on days 1 through 7. Allopurinol therapy to start 48 hours prior to Chemotherapy. Repeat courses after marrow recovery, the total number of courses not to exceed 3.

Arm I: ARA-C - 200 mg/sqm/day sc in 2 divided doses; TG - 200 mg/sqm/day po in 2 divided doses. Continue treatment until bone marrow aplasia is achieved, usually 10-12 doses. Repeat course at 10-week intervals.

Arm II: ARA-C and TG as in Arm I; Neuraminidase-treated allogeneic myeloblasts as soon as adequate hematologic recovery from Chemotherapy has occurred, with a second treatment exactly 4 weeks after the first. Second dose of Chemotherapy to be given 14 days after the second Immunotherapy treatment.

Arm III: ARA-C and TG as in Arm I. Splenectomy to occur immediately following recovery from first course of Maintenance Chemotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

6.0044 PHASE II CHEMOTHERAPY WITH AMSA FOR PREVIOUSLY TREATED ACUTE NONLYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) BCRP-7810

OBJECTIVES:

I. Ascertain the efficacy of m-AMSA for remission induction in previously treated, relapsed or initially refractory patients with acute nonlymphocytic leukemia.

PROTOCOL ENTRY CRITERIA: Acute nonlymphocytic leukemia patients ineligible for protocols BCRP 7802 and 7707. Patients may be refractory to antimetabolites, anthracyclines, cytosine arabinoside, and L-asparaginase combinations.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: None given.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: AMSA - 60 mg/sqm iv infusion over 45 minutes daily until marrow hypoplasia is achieved. Dose increased to 70 mg/sqm/day if hypoplasia not achieved by day 14. Stop treatment if marrow hypoplasia is not achieved by day 21 and declare patient resistant to AMSA. Observe for 1-2 weeks and if marrow does not improve, institute alternate chemotherapy. Initial dose of AMSA will be increased to 70 mg/sqm if 3 of the first 5 patients on study do not achieve hypoplasia by day 14. Repeat courses at 1-4 week intervals from the last dose. If after 3 courses there is no demonstrable antileukemic response and/or life-threatening toxicity intervenes, the patient will go off study.

Consolidation: Within 1 week of achieving CR give the first of 2 consolidation courses consisting of a single daily injection of AMSA for 2/3 the number of days required for Induction (minimum 5 days). Repeat in 1 month. No further therapy until relapse.

If relapse occurs within 3 months from the last AMSA therapy, treat with alternative therapy. If remission is greater than 3 months, attempt to reinduce with the same AMSA dose and schedule used for first induction.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

6.0045 LATE INTENSIFICATION WITH CROP (CTX/RBD/VCR/PRED) WITH OR WITHOUT ACTIVE SPECIFIC IMMUNOTHERAPY FOR AML

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PROTOCOL NUMBER(S) MDAR-239; MDA-DT-7745

OBJECTIVES:

I. Determine the efficacy of late intensification combination chemotherapy with cyclophosphamide (CTX), rubidazone (RBD), vincristine (VCR), and prednisone (PRED) followed by active specific immunotherapy in preventing subsequent relapse in acute myeloblastic leukemia patients less than 50 years of age who are in complete remission.

II. Determine the toxicity of this regimen administered in intermittent courses.

III. Determine whether serial bone marrow kinetics, chromosome condensation, changes in immunocompetence or levels of serum immune complexes and (possibly in the future) colony formation techniques can be utilized as early predictors of leukemic relapse.

IV. Determine in a Phase II study the effect of active specific immunotherapy with pooled allogeneic leukemia antigen on the following immunological parameters: (1) skin test response to leukemia antigen; (2) antibody to leukemia specific antigen determined by radioimmunoassays and by immunoglobulin binding to autologous or allogeneic leukemic blast cells; (3) blastogenic responses to allogeneic and autologous leukemia blasts; (4) lymphocyte cytotoxicity to autologous and allogeneic leukemic cells.

V. Determine the feasibility of utilizing a vaccine consisting of tumor antigen and adjuvant to immunize patients after late-intensification chemotherapy.

VI. Determine the effect of active specific immunization on remission duration and survival.

PROTOCOL ENTRY CRITERIA: Patients under age 50 with histologically confirmed acute myeloblastic leukemia in complete remission for at least 6 months on protocol MDAR-155 (DT-76 06) or MDAR-251 (DT-77 24). Patients' bone marrow must have less than 5% blasts and less than 10% blasts plus promyelocytes. Circulating blood must be free of leukemic cells and blood counts must be adequate. Patients must not have received more than 300 mg/sqm of adriamycin or equivalent anthracycline.

PROTOCOL OUTLINE: Study randomized for Immunotherapy. Following late Intensification and Maintenance on MDAR-155 or

Regimen A: 3-Drug Combination Chemotherapy plus Hormone Therapy. CROP: Cyclophosphamide, CTX, NSC-26271; Rubidazone, RBD, NSC-164011; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Arm I: Immunotherapy. Leukemia antigen plus CWS-P3 adjuvant.

Arm II: No further therapy.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Duration of remission, toxicity rate, survival rate.

CURRENT STATUS: About 30 patients/year will be entered.

DOSAGE SCHEDULE:

Arm I: CROP: CTX - 1000 mg/sqm iv on day 1; RBD - 200 mg/sqm iv (100 mg/sqm for patients with poor liver function) on day 1; VCR - 1.4 mg/sqm iv (maximum dose 2.0 mg) on day 1; PRED - 100 mg/day po on days 1 through 5. Repeat course q 3 to 4 weeks for a total of 3 courses.

Arm II: Leukemia antigen - 400 micrograms admixed with 50 micrograms CWS-P3 adjuvant given id q month, rotating the injection between arms and legs.

Arm III: No further therapy.

Follow all patients until relapse as defined by more than 5% leukemic cells or more than 10% leukemic cells plus promyelocytes in the bone marrow.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

6.0046 ADOAP INDUCTION PLUS ARA-C/TG MAINTENANCE IN PEPA WITH WBC TRANSFUSIONS FOR ADULT ACUTE MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) MDAR-251; MDA-DT-7771

OBJECTIVES:

I. Determine whether protected environments plus prophylactic antibiotics (PEPA) and white blood cell (wbc) transfusions permit more intensive chemotherapy with ADOAP - adriamycin (ADR)/cytosine arabinoside (ARA-C) vincristine (VCR)/prednisone (PRED) - during remission induction of acute leukemia.

II. Determine the efficacy of wbc transfusions in reducing the risk of infection.

III. Determine the efficacy of intensive remission induction chemotherapy in increasing the duration of remission.

PROTOCOL ENTRY CRITERIA: Previously untreated patients less than 50 years of age with absolute leukemic infiltration over 50% or with less than 50% infiltration but progressive disease.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Adriamycin, ADR, NSC-123127; Cytosine arabinoside, ARA-C, NSC-63878; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; plus PEPA and/or wbc transfusions as available.

Maintenance: 2-Drug Combination Chemotherapy. ARA-C plus Thioguanine, TG, NSC-752.

Intensification: CROP: 3-Drug Combination Chemotherapy plus Hormone Therapy. Cyclophosphamide, CTX, NSC-26271; Rubidazone, RBD, NSC-164011; VCR; PRED.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Bone marrow and peripheral blood remission, response/remission rate, duration of remission.

CURRENT STATUS: 80 patients will be entered in about 2.5 years.

[illegible]

Induction: ADOAP: ADR - 55 mg/sqm iv on day 1; ARA-C - 90 mg/sqm iv on days 1 through 7; VCR - 2 mg iv on day 1; PRED - 100 mg po on days 1 through 5. (Duration of course and number to be given are not stated.) Escalate ADR to 75 mg/sqm and ARA-C to 120 mg/sqm during courses 2 and 3. If available, use PEPA and/or wbc transfusions after last 2 courses, beginning 48 hours or less after circulating granulocytes fall below 500/cumm and continue for at least 5 transfusions in 9 days.

Maintenance: ARA-C - 150 mg/sqm sc on days 1 through 5; TG - 100 mg/sqm/day in two divided doses (route not given) on days 1 through 5. Give a total of 3 courses.

Intensification: CROP: CTX; RBD; VCR; PRED (dosages not given). See MDAR-239, MDA-DT-7745.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

6.0047 TREATMENT OF RELAPSED CHILDHOOD ACUTE NONLYMPHOCYTIC LEUKEMIA WITH HIGH-DOSE MTX AND LEUCOVORIN RESCUE FOLLOWED BY AMSA

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PROTOCOL NUMBER(S) SJCRH-AML-R

OBJECTIVES:

I. Evaluate the efficacy of high-dose methotrexate and leucovorin rescue followed by AMSA in the treatment of children with acute nonlymphocytic leukemia who have relapsed after starting Intensification therapy with VP-16213 plus 5-azacytidine.

II. Kill and synchronize leukemic blasts in vivo in S phase with a prolonged infusion of methotrexate.

III. Selectively kill leukemic blasts in S phase while sparing normal marrow cells by administering AMSA 48 hours after the methotrexate infusion.

IV. Determine the pharmacokinetics of AMSA and its metabolites.

PROTOCOL ENTRY CRITERIA: Children with acute nonlymphocytic leukemia who, during Intensification therapy with VP-16213 and 5-azacytidine, have experienced a relapse.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590; m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Bone marrow cell kinetic studies, cell culture studies, serum pharmacokinetic studies.

END POINTS: Remission rate, duration of complete remission.

CURRENT STATUS: 25 patients will be entered over 2 years.

DOSAGE SCHEDULE:

MTX - 200 mg/sqm iv push followed by 1200 mg/sqm iv over 36 hours; CF - 30 mg/sqm iv at 2, 6, 12, 18, and 23 hours after completion of the MTX infusion, then 3 mg/sqm po q 8 hours for 6 doses; AMSA - 200 mg/sqm iv over 30-45 minutes daily for 3 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 12/80

6.0048 INTENSIVE SEQUENTIAL ADR/ARA-C, VP-16/AZC, 6-TG/ARA-C, AND ADR/ARA-C AFTER INDUCTION WITH DNM/ARA-C FOR CHILDHOOD ACUTE NONLYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) SJCRH-AML-80

I. Determine whether duration of CR in children with acute nonlymphocytic leukemia (ANLL) is significantly prolonged by the administration sequentially of 2-drug combinations in maximally tolerated doses using adriamycin/cytosine arabinoside, VP-16/5-azacytidine, 6-thioguanine/cytosine arabinoside, and adriamycin/cytosine arabinoside.

II. Identify nonresponders and patients destined to have short remissions through changes in leukemia cell kinetics during the first 5 days of therapy.

III. Study the pharmacokinetics of adriamycin.

IV. Compare the therapeutic effect of bone marrow transplantation in remission vs. no bone marrow transplantation in children with ANLL given identical Induction therapy on a controlled therapy protocol.

PROTOCOL ENTRY CRITERIA: Previously untreated patients under the age of 20 years who have ANLL. Patients may have had up to 6 days of prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study. Enter all patients on Regimen A. Enter patients without evidence of CNS involvement on Regimen B and those with overt CNS disease on Regimen C. Enter patients with an HLA-identical bone marrow donor on Regimen D and those without a donor on Regimen E.

Regimen A: Induction. 2-Drug Combination Chemotherapy. Daunomycin, DNM, NSC-82151; Cytosine arabinoside, ARA-C, NSC-63878.

Regimen B: CNS Prophylaxis. Single-agent Intrathecal Chemotherapy. Methotrexate, MTX, NSC-740.

Regimen C: CNS Treatment. Single-agent Intrathecal Chemotherapy. MTX.

Regimen D: Bone Marrow Transplantation.

Regimen E: Intensification Therapy. 5-Drug Combination Chemotherapy in 2-Drug Sequential Combinations. Adriamycin, ADR, NSC-123127; ARA-C; followed by VP-16213, VP-16, NSC-141540; 5-Azacytidine, AZC, NSC-102816; followed by 6-Thioguanine, 6-TG, NSC-752, ARA-C; followed by ADR; ARA-C.

STRATIFICATION BY: Presence of overt CNS involvement at diagnosis (yes vs. no), availability of HLA-identical bone marrow donor (yes vs. no).

SPECIAL STUDY PARAMETERS: Hematologic parameters, microbiological cultures, chest x-ray, EKG, echocardiogram, liver and kidney function tests, immunoglobulins, electrolytes, bone marrow for cytology and cell profile, kinetic and pharmacokinetic studies on marrow and blood, CSF examination, coagulation screen, antibody titers for hepatitis B and monoslide test, skin tests, radiographs and scans as indicated clinically.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: About 75 patients will be entered over 3 years.

DOSAGE SCHEDULE:

Regimen A: DNM - 45 mg/sqm iv push on days 1 through 3; ARA-C - 100 mg/sqm/day by continuous iv or sc infusion on days 4 through 10. If bone marrow on day 14 shows more than 5 percent leukemic cells, give a second Induction course with DNM on days 1 and 2 and ARA-C on days 1 through 5. If leukemic cells are less than 5 percent, withhold Chemotherapy until marrow recovery or progression and give the second course of Induction Chemotherapy after platelets are greater than 100,000 and neutrophils greater than 500. All patients in remission after 2 Induction courses proceed to Regimen D or E.

Regimen B: MTX - 12 mg/sqm (maximum 12 mg) it monthly for 6 months beginning 4 weeks after diagnosis, then q 3 months until all therapy is withdrawn. Patients on Regimen D continue it MTX monthly following transplant for 5 months, then q 3 months for 2 doses.

Regimen C: MTX - 12 mg/sqm (maximum 12 mg) it weekly until CSF is clear, then monthly until therapy is withdrawn.

Regimen D: Bone marrow transplant as soon as patient has recovered from 2 courses of Induction therapy, within 1 month of

Regimen E: ADR - 45 mg/sqm iv push on day 1; ARA-C - 200 mg/sqm/day by continuous iv or sc infusion on days 1 through 5; repeat courses q 21-25 days for the first 3 months after recovery from 2 courses of Induction therapy. VP-16 - 200 mg/sqm iv push on days 1, 2, 3, 8, 9, and 10; AZC - 300 mg/sqm iv over 45 minutes on days 4, 5, 11, and 12; repeat course q 28 days for the second 3 months. 6-TG - 200 mg/sqm po in 2 divided doses on days 1 through 5; ARA-C - 200 mg/sqm/day by continuous iv or sc infusion on days 1 through 5; repeat course q 21-25 days for the third 3 months. ADR - 45 mg/sqm/day iv push on day 1; ARA-C - 200 mg/sqm/day by continuous iv or sc infusion on days 1 through 5; repeat q 21-25 days for the fourth 3 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

6.0049 CHEMOTHERAPY WITH TAD (6-TG/ARA-C/DNM), ADR, AZC PLUS IMMUNOTHERAPY WITH C. PARVUM, ALLOGENEIC LEUKEMIC BLASTS FOR ACUTE MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) UCLA-ALP-3

OBJECTIVES: This protocol supersedes ALP-1.

I. Evaluate the efficacy of intensive Induction chemotherapy with cytosine arabinoside (ARA-C), thioguanine (6-TG), daunomycin (DNM) in AML.

II. Evaluate the efficacy of immunotherapy vs. no immunotherapy in remission maintenance in AML (randomized).

III. Evaluate the role of Maintenance chemotherapy in AML (retrospective).

PROTOCOL ENTRY CRITERIA: Patients with AML who are at least 3 years of age.

PROTOCOL OUTLINE: Patients randomized following Induction and Consolidation.

Induction:

3-Drug Combination Chemotherapy. TAD: Cytosine arabinoside, ARA-C, NSC-63878; Daunomycin, DNM, NSC-82151; 6-Thioguanine, 6-TG, NSC-752.

Consolidation:

1st cycle: Adriamycin, ADR, NSC-123127; Azacytidine, AZC, NSC-102816. 2nd cycle: TAD. Randomize to Arm I or Arm II.

Arm I: No further therapy.

Arm II: Immunotherapy. Intralymphatic allogeneic leukemic blasts plus Corynebacterium parvum, C. parvum, unspecified.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Remission, survival.

CURRENT STATUS: More than 50 patients have been entered as of February 1980.

DOSAGE SCHEDULE: No details given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

6.0050 CHEMOTHERAPY WITH ARA-C VS ARA-C/TG VS ARA-C/DNM FOR INDUCTION AND METHYL GAG OR ARA-C FOR MAINTENANCE IN ACUTE MYELOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) EORTC-LAM-2

OBJECTIVES

I. Compare the frequency of complete remissions obtained with

II. Determine the efficacy of a complementary chemotherapy, or maintenance once remission is obtained.

PROTOCOL ENTRY CRITERIA: Patients of all ages and both sexes with acute myeloblastic leukemia.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I: Single-agent Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878.

Arm II: 2-Drug Combination Chemotherapy. Thioguanine, TG, NSC-752; ARA-C.

Arm III: 2-Drug Combination Chemotherapy. Daunomycin, DNM, NSC-82151; ARA-C.

Maintenance: Ènter patients who have achieved complete remission.

Arm IV: Single-agent Chemotherapy. Methyl GAG, MeGAG, NSC-32946.

Arm V: Single-agent Chemotherapy. ARA-C.

STRATIFICATION BY: Age: 0-15 years, 15-60 years, above 60; percentage of granulocytic leukemic cells in the bone marrow: 5-15%, 15-50%, over 50%.

SPECIAL STUDY PARAMETERS: Myelogram, liver function tests.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, remission duration.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction:

Arm I: ARA-C - 100 mg/sqm iv q 12 hours x 7 to 10 days for a total of 14 to 20 injections. Rest 2 to 3 weeks, then repeat therapy and rest period for 1 or 2 additional courses.

Arm II: TG - 80 mg/sqm po q 12 hours x 7 to 10 days. Give the first dose 6 hours before the first dose of ARA-C. ARA-C - 100 mg/sqm iv q 12 hours x 7 to 10 days. Repeat TG and ARA-C therapy for 1 or 2 courses with a 2-to-3-week rest period between each course.

Arm III: DNM - 60 mg/sqm on day 1; ARA-C - as in Arm I beginning on day 2 and continuing for 7 to 10 days. Rest 2-3 weeks, then repeat therapy and rest period for 1 or 2 additional courses. Continue therapy for a minimum of 3 courses for nonresponders or until remission is achieved for responders.

Maintenance: Enter patients in complete remission following Induction to Arm IV or Arm V.

Arm IV: MeGAG - 200 mg/sqm iv once a week in a serum glucose infusion.

Arm V: ARA-C - 120 mg/sqm sc once a week.

Duration of maintenance treatment is not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

6.0051 CHEMOTHERAPY WITH ARA-C AND VCR FOLLOWED BY DNM, THEN ARA-C/MEGAG AND/OR IMMUNOTHERAPY FOR ACUTE MYELOBLASTIC LEUKEMIA

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PROTOCOL NUMBER(S) EORTC-LAM-3

OBJECTIVES:

I. Compare four chemotherapeutic regimens with cytosine arabinoside (ARA-C) with or without vincristine (VCR) for remission induction in acute myeloblastic leukemia (AML).

II. Evaluate consolidation therapy with daunomycin (DNM) for responders to induction therapy.

III. Compare maintenance with ARA-C/methyl GAG (MeGAG) chemotherapy plus immunotherapy with BCG and irradiated leuke-

PROTOCOL ENTRY CRITERIA: Patients in the early stage of acute myelocytic leukemia who have not received prior chemotherapy except for prednisone for 7 days or a cytostatic drug other than those in this protocol for a maximum of 5 days.

PROTOCOL OUTLINE: Study randomized for Induction and Maintenance. Patients with myeloblastic proliferation who fail to respond to Induction therapy enter Regimen A. Failures with monoblastic proliferation enter Regimen B. Failures on Regimens A and B proceed to Regimen C; patients showing a complete response enter Maintenance Arm VI. Patients who respond to Induction proceed to Consolidation and are then rerandomized for Maintenance.

Induction: Arms I, II, III and IV.

Arm I: 2-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Cytosine arabinoside, ARA-C, NSC-63878.

Arm II: 2-Drug Combination Chemotherapy. ARA-C; VCR.

Arm III: Single-agent Chemotherapy. ARA-C, 12-hour infusion.

Arm IV: Single-agent Chemotherapy. ARA-C, 24-hour infusion.

Regimen A: Single-agent Chemotherapy. Daunomycin, DNM, NSC-82151.

Regimen B: Single-agent Chemotherapy. VP-16213, VP-16, NSC-14150.

Regimen C: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Consolidation: Single-agent Chemotherapy. DNM.

Maintenance:

Arm V: 2-Drug Combination Chemotherapy. ARA-C; Methyl GAG, MeGAG, NSC-32946.

Arm VI: Immunotherapy. BCG, plus irradiated leukemic cells.

Arm VII: 2-Drug Combination Chemotherapy plus Immunotherapy. ARA-C; MeGAG as in Arm V plus BCG; irradiated leukemic cells as in Arm VI.

STRATIFICATION BY: Age, more or less than 60 years old; for nonresponders to Induction: morphologic subtypes.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, survival rate, duration of survival, duration of remission.

CURRENT STATUS: 232 patients will be entered.

DOSAGE SCHEDULE:

Prior to Chemotherapy, collect leukemic cells for cryopreservation and Maintenance Immunotherapy (Supplement, May, 1974).

Induction: Repeat all courses for one additional cycle.

Arm I: VCR - 1 mg/sqm/day iv at 8 PM on days 1 and 2; ARA-C - 240 mg/sqm/day by continuous iv infusion from 8 AM to 8 PM on days 3 through 7. Rest 10 to 14 days.

Arm II: ARA-C - 240 mg/sqm/day by continuous iv infusion from 8 AM to 8 PM on days 1 through 5; VCR - 1 mg/sqm/day iv at 8 PM on days 6 and 7. Rest 10 to 14 days.

Arm III: ARA-C - 240 mg/sqm/day by continuous iv infusion from 8 AM to 8 PM on days 1 through 5. Rest 10 to 14 days.

Arm IV: ARA-C - 240 mg/sqm/day by continuous 24-hour iv infusion on days 1 through 5. Rest 10 to 14 days.

Evaluate all patients after 2 courses in each arm. Give all complete or partial responders in Arms I through IV one additional course of their Induction therapy; if response is still partial (regression without remimission) give a 4th course and re-evaluate. Enter failures to Regimen A or Regimen B according to cell type.

Regimen A: DNM - 100 mg/sqm/day for 3 days. Rest 8 days, then repeat 3-day course.

Regimen B: VP-16 - 60 mg/sqm/day iv on days 1 through 5. Rest 8 days. Repeat 5-day course.

Regimen C: ADR - 30 mg/sqm/day (route not given) on days 1 and 2.

Consolidation: DNM - 60 mg/sqm/day on days 1, 2 and 3. Rest 14 days, then repeat course.

Maintenance:

Arm V: ARA-C - 100 mg/sqm sc on days 1 through 7. MeGAG -

Arm VI: Begin 4 months after last chemotherapeutic dose and continue until relapse. BCG - no details given, plus cryopreserved irradiated leukemic cells prepared as described in supplement (May, 1974), given once a week for 6 weeks, then once q 14 days for 6 weeks, then once q 4 weeks.

Arm VII: ARA-C plus MeGAG, as in Arm V, plus BCG plus irradiated leukemic cells, as in Arm VI.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

6.0052 PHASE II-III CHEMOTHERAPY WITH ADR/VCR/ARA-C PLUS IMMUNOTHERAPY WITH BCG AND IRRADIATED CELLS FOR ACUTE MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) EORTC-LAM-4

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with ADR/VCR/ARA-C in Phase II treatment of acute myelogenous leukemia.

II. Determine the influence of reinforcement therapy with ADR/ARA-C on the duration of remission in a Phase III study.

III. Determine the differences in extent of remissions obtained with immunotherapy alone, chemotherapy alone or with combination chemoimmunotherapy.

IV. Investigate whether partial responders following three remission induction courses may be brought into complete remission by prolongation of the induction course.

PROTOCOL ENTRY CRITERIA: Patients less than 60 years of age with acute myelogenous leukemia. Patients may be in early stages of the disease and may have more than 30% blast cells in the bone marrow.

PROTOCOL OUTLINE: Study randomized for Reinforcement and Maintenance. Enter all patients to Induction. Complete responders are randomized to Arms I and II. Responders are then rerandomized to Maintenance Arms III, IV, and V.

Induction: 3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Cytosine arabinoside, ARA-C, NSC-63878.

Reinforcement:

Arm I: 2-Drug Combination Chemotherapy. ADR; ARA-C.

Arm II: Control. No Reinforcement Therapy.

Maintenance:

Arm III: Immunotherapy. Pasteur BCG, BCG, NSC-B116328, plus irradiated leukemic cells.

Arm IV: 2-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037.

Arm V: 2-Drug Combination Chemotherapy plus Immunotherapy. CTX; CCNU; plus BCG and irradiated leukemic cells.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Bone marrow, skin tests including Candida, mumps, PPD.

END POINTS: Response/remission rate, duration of remission.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: ADR - 50 mg/sqm iv on day 1 (maximum cumulative dose 300 mg/sqm); VCR - 1 mg/sqm iv on day 2; ARA-C - 40 mg/sqm/day iv in 2 divided doses q 12 hours on days 3 through 8. Repeat course q 15 days for a total of 2 or 3 courses. After 3 courses, partial responders receive 2 more courses with ARA-C given on days 3 through 9. Randomize complete responders to Reinforcement, Arm I or Arm II.

Reinforcement:

Arm I: Continue ADR, plus ARA-C, as in Induction. Give 2 additional courses.

Arm II: No Reinforcement Therapy.

– Maintenance: Begin therapy 15 days following Arm I Reinforcement, or 15 days following Induction therapy for patients randomized to Arm II.

Arm III: BCG - 1 x ten to the ninth viable units/ml 3x/week in the 1st week, 2x/week in the 2nd week and 3rd week, and once a week thereafter. BCG is applied to one scarification area in anergic patients and to four scarification areas in allergic patients. Irradiated pooled blast cells obtained from patients with untreated acute myeloblastic leukemia - 5 x 10 to the seventh cells mixed with 1 ampule of BCG and applied once a week together with the last BCG treatment. Duration of Immunotherapy not given.

Arm IV: CTX - 1000 mg/sqm/day iv q 8 weeks administered simultaneously with CCNU - 200 mg/sqm/day po (maximum cumulative dose 300 mg).

Arm V: CTX and CCNU, as in Arm IV. Three weeks after 1st dose of Chemotherapy, give BCG and irradiated leukemic cells, as in Arm III, for 1 week. Duration of therapy not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

6.0053 COMPARISON OF MAINTENANCE COMBINATIONS FOLLOWING ADR/VCR/ARA-C INDUCTION FOR AML

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PROTOCOL NUMBER(S) EORTC-06781

OBJECTIVES:

I. Verify in a non-randomized trial if the combination adriamycin (ADR), vincristine (VCR), and cytosine arabinoside (ARA-C) is effective in inducing a high rate of complete remission in patients with AML.

II. Compare in complete responders to above Induction therapy alternative Maintenance treatments with: 6-mercaptopurine (6-MP), methotrexate (MTX), reinforced with VCR/daunomycin (DNM) vs. 6-MP/MTX/VCR/DNM plus stanozolol vs. 6-thioguanine (TG)/ARA-C vs. TG/ARA-C plus immunotherapy with allogenic leukemia cells treated with neuraminidase.

PROTOCOL ENTRY CRITERIA: Patients between 10 and 65 years of age with histologically diagnosed acute (excluding pro-) myelocytic, myeloblastic, or monocytic leukemia confirmed by WHO reference center (R.C.). Patients must not have had prior therapy by any drugs used in this study nor more than one week of corticosteroid therapy.

PROTOCOL OUTLINE: All patients enter Induction; responders are randomized for Maintenance.

Induction: 3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Cytosine arabinoside, ARA-C, NSC-63878.

Maintenance:

Arm I: 4-Drug Combination Chemotherapy. 6-Mercaptopurine, 6-MP, NSC-755; Methotrexate, MTX, NSC-740; VCR; Daunomycin, DNM, NSC-82151.

Arm II: 5-Drug Combination Chemotherapy. 6-MP; MTX; VCR; DNM; plus Stanozolol, NSC-43193.

Arm III: 2-Drug Combination Chemotherapy. 6-Thioguanine, TG, NSC-752; ARA-C.

Arm IV: 2-Drug Combination Chemotherapy plus Immunotherapy. TG; ARA-C; plus allogenic myeloblasts treated with Neuraminidase

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Bone marrow evaluation.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, length of survival, survival time, disease-free interval.

CURRENT STATUS: 435 patients will be entered for Induction therapy and 304 patients will be entered for Maintenance therapy.

DOSAGE SCHEDULE:

Induction: ADR - 50 mg/sqm iv on day 1; VCR - 1 mg/sqm iv on day 2; ARA-C - 80 mg/sqm iv push q 12 hours on days 3 through 9. Examine bone marrow 15 to 21 days after end of cycle. All patients receive 2 courses. Complete responders (based on bone marrow evaluation) then proceed to Maintenance. Patients showing a partial response or no response receive a 3rd course. Patients showing no response after the 3rd course go off study; responders receive a 4th course and are randomized for Maintenance.

Maintenance: Therapy begins 2 to 4 weeks after the last course of Induction therapy.

Arm I: 6-MP - 70 mg/sqm po on days 1 through 14; MTX - 15 mg/sqm im 2 times/week on days 15 through 28; VCR - 1 mg/sqm iv and DNM - 35 mg/sqm iv on day 28. Repeat every 28 days until relapse except give DNM/VCR only at the end of course 1, 3, 6, 10, and 14.

Arm II: 6-MP, MTX, VCR, DNM, as in Arm I, plus Stanozolol - 0.5 mg/kg/day po.

Arm III: TG - 70 mg/sqm/day po on days 1 through 4; ARA-C - 80 mg/sqm sc on day 5. Repeat course q 7 days until relapse.

Arm IV: TG and ARA-C. as in Arm III, for 4 courses, then rest 21 days. On day 11 of rest, give Immunotherapy: 10 to the ninth power allogenic myeloblasts previously collected from patient or donor and freshly suspended with neuraminidase given id to one of 4 injection sites.

Repeat therapy plus rest until relapse. Recommended duration of Maintenance: 4 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/79

6.0054 COMBINATION CHEMOTHERAPY WITH ARA-C/DNM/TG PLUS IMMUNOTHERAPY WITH MER-BCG FOR ACUTE NONLYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) ISR-ANLL-1

OBJECTIVES:

I. Prolong first remission in patients with acute nonlymphocytic leukemia and facilitate Induction of second remission to prolong length of survival by combination chemotherapy using cytosine arabinoside (ARA-C)/daunomycin (DNM)/6-thioguanine (TG) plus Immunotherapy with MER-BCG (MER).

PROTOCOL ENTRY CRITERIA: Patients below the age of 65 with ANLL in M1 remission.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Immunotherapy. Cytosine arabinoside, ARA-C, NSC-63878; 6-Thioguanine, TG, NSC-752; Daunomycin, DNM, NSC-82151; MER-BCG, MER, NSC-143769.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Monthly assessment of immune response by: PHA, Con-A- and allogenic lymphocyte-induced transformation; skin reactivity to KLH; 19S and 7S antibody titer against KLH.

END POINTS: Length of survival.

CURRENT STATUS: 83 patients have been entered as of February 1980; protocol open to patient entry until December 1981.

DOSAGE SCHEDULE:

Induction: ARA-C - 100 mg/sqm iv q 12 hours on days 1 through 5; TG - 100 mg/sqm po q 12 hours on days 1 through 5; DNM - 60 mg/sqm iv on days 6 through 8. Rest 14 days. Repeat up to 3 times if necessary. Maintenance: 3 weeks after remission, 2-drug administration in 5-day courses monthly for 18 months. Consolidation: At 11 months, ARA-C, TG, DNM as in Induction. MER is administered intracutaneously into the back in monthly doses of 0-2 mg beginning 3 weeks after remission is achieved for 20 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

6.0055 CHEMOTHERAPY WITH ARA-C/DRB/TG, ARA-C/VCR/ADR, AND DRB/ARA-C/TG/VCR/DMX WITH OR WITHOUT BCG IMMUNOTHERAPY FOR AML

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PROTOCOL NUMBER(S) ITA-AIL-7801

OBJECTIVES:

I. Compare remission, duration of remission and survival using combination chemotherapies: cytosine arabinoside (ARA-C)/daunorubicin (DRB)/6-thioguanine (TG); adriamycin (ADR)/ARA-C/vincristine (VCR) and dexamethasone (DMX)/DRB/TG/VCR/ARA-C with and without MER-BCG in remission Induction, Consolidation and Maintenance regimens.

II. Determine the morbidity, toxicity, and immunologic changes caused by MER-BCG administration.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with acute nonlymphoblastic leukemia between the ages of 3 and 65 years with no more than 7 days corticosteroid therapy and without signs of systemic infection. BUN must be less than 40 mg percent and creatinine less than 1.5 mg percent.

PROTOCOL OUTLINE: All patients are randomized to Arms I and II for remission Induction. Patients achieving remission are re-randomized to Arms III and IV for Consolidation.

Induction:

Arm I: 3-Drug Combination Chemotherapy plus Immunotherapy. Daunorubicin, DRB, NSC-82151; Cytosine arabinoside, ARA-C, NSC-63878; Thioguanine, TG, NSC-752; plus MER-BCG, BCG, NSC-143769.

Arm II: 3-Drug Combination Chemotherapy. DRB; ARA-C; TG.

Consolidation:

Arm III: 3-Drug Combination Chemotherapy plus Immunotherapy. ARA-C; Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; plus BCG. Patients entered to Arm V for Maintenance.

Arm IV: 3-Drug Combination Chemotherapy. ARA-C; VCR; ADR. Patients entered to Arm VI for Maintenance.

Maintenance:

Arm V: 5-Drug Combination Chemotherapy plus Immunotherapy. DRB; ARA-C; TG; VCR; Dexamethasone, DM, NSC-34521; plus BCG.

Arm VI: 5-Drug Combination Chemotherapy. DRB; ARA-C; TG; VCR; DM.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Lymphocyte populations; lymphoblastogenesis: PHA, PWM; serum immunoglobulin levels; skin tests: PPD, mumps, dermatophytin 'O', varidase.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 47 patients have been entered in 2 years.

DOSAGE SCHEDULE:

Induction:

Arm I: DRB - 80 mg/sqm iv on day 1; ARA-C - 240 mg/sqm iv on days 2 through 6; TG - 240 mg/sqm po on days 2 through 6; BCG - 200 micrograms id at 5 sites for total dose of 1 mg on day 1. Rest 10 days. Repeat course once.

Arm II: DRB, ARA-C and TG as in Arm I.

Consolidation: Rerandomize responders from Induction therapy.

Arm III: VCR - 1.5 mg/sqm iv on afternoon of day 1; ADR - 20 mg/sqm iv on days 2 through 3; ARA-C - 100 mg/sqm iv on days 2 through 4; VCR - 1 mg/sqm iv on day 5; BCG - 200 micrograms at 5 sites id on day 17. Rest for 11 days, followed by Arm V Maintenance.

Arm IV: VCR; ADR; ARA-C as in Arm III, followed by Arm VI Maintenance.

Maintenance:

Arm V: 3 alternating 5-day courses of Chemotherapy q 4 weeks. BCG - 200 micrograms at 5 sites id on day 17 of each 28-day cycle. (1) ARA-C - 200 mg/sqm sc on days 1 through 5, TG - 200 mg/sqm po on days 1 through 5. (2) ARA-C - 200 mg/sqm sc on days 1 through 5; VCR - 1.5 mg/sqm iv on day 1; DM - 8 mg/sqm po on days 1 through 5. (3) ARA-C - 200 mg/sqm sc on days 1 through 5. DRB - 45 mg/sqm iv on days 1 and 2.

Arm VI: Chemotherapy as in Arm V. (1) ARA-C; TG. (2) ARA-C; VCR; DM. (3) ARA-C; DRB.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 1.25 mg vials; DRB - 20 mg vials; ARA-C - 100 mg vials; TG - 40 mg tablets; VCR - 1 mg vials; ADR - 10 mg vials; DM - 0.5 and 0.75 mg tablets.

DATE SUMMARIZED: 08/80

6.0056 PHASE II MAINTENANCE CHEMOTHERAPY WITH AND WITHOUT IMMUNOTHERAPY WITH NOCARDIA RUBRA-CWS WITH AND WITHOUT ALLOGENEIC LEUKEMIA CELLS FOR ANLL

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PROTOCOL NUMBER(S) JAP-ANLL-N-CWS-2

OBJECTIVES:

I. Evaluate the clinical efficacy of chemoimmunotherapy with Nocardia rubra-Cell Wall Skeleton (N-CWS) in patients with acute nonlymphocytic leukemia (ANLL) in remission.

II. Confirm the in vivo and in vitro effectiveness of N-CWS on the host immune response.

PROTOCOL ENTRY CRITERIA: Patients 15 to 60 years of age, in complete remission from ANLL, without infection or hepatic dysfunction.

PROTOCOL OUTLINE: Randomized study. Following two courses of Consolidation Chemotherapy (details not given), patients in first complete remission are randomized to Maintenance arms.

Maintenance:

Arm I: 6-Drug Combination Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878; Daunomycin, DNM, NSC-82151; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; 6-Mercaptopurine-riboside, 6-MP-R, NSC-4911; Methotrexate, MTX, NSC-740.

Arm II: 6-Drug Combination Chemotherapy plus Immunotherapy. ARA-C; DNM; CTX; VCR; 6-MP-R; MTX; plus Nocardia rubra - Cell Wall Skeleton, N-CWS.

Arm III: 6-Drug Combination Chemotherapy plus Immunotherapy plus irradiated tumor cells. Arm I plus Arm II, plus irradiated allogeneic leukemia cells.

STRATIFICATION BY: Age, sex, type of leukemia.

SPECIAL STUDY PARAMETERS: Skin tests, cell-mediated cytotoxicity to allogeneic tumor cells (AL-1), NK activity.

END POINTS: Remission duration, survival time, toxicity of treatment.

CURRENT STATUS: 40 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Maintenance:

Arm I: ARA-C - 1 mg/kg iv monthly; DNM - 0.5 mg/kg iv monthly; CTX - 5 mg/kg iv monthly; VCR - 1 mg/day; 6-MP-R - 3 mg/kg po for 7 days/month; MTX - 10 mg/day po for 7 days/month.

Arm II: ARA-C; DNM; CTX; VCR; 6-MP-R; MTX - all as in Arm I. N-CWS - 300 micrograms id initially, then 200 micrograms biweekly for 8 weeks, then monthly. Chemotherapy withheld for 4 weeks following initial dose of N-CWS, then given at intervals of each N-CWS injection as in Arm I.

Arm III: ARA-C; DNM; CTX; VCR; 6-MP-R; MTX; N-CWS - all as in Arm II. Irradiated (10,000 rad) allogeneic leukemia cells - 5 x 10 to the seventh id with initial dose of N-CWS. Chemotherapy withheld for 4 weeks following initial dose of N-CWS, then given at intervals of each N-CWS injection as in Arm I.

Dosage modifications for toxicity are given.

Summary as provided by investigator.

DOSAGE FORMS: N-CWS - 1 and 2 mg vials; CTX - 100 mg vials; DNM - 20 mg vials; 6-MP-R - 100 mg powders; VCR - 1 mg vials; MTX - 2.5 mg tablets; ARA-C - 20 mg vials.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00400280

6.0057 COMBINATION CHEMOTHERAPY WITH OR WITHOUT BONE MARROW TRANSPLANT AND LONG-TERM VS SHORT-TERM MAINTENANCE IN ANLL

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PROTOCOL NUMBER(S) SAFR-ANLL-1

OBJECTIVES:

I. Compare survival rate after bone marrow transplantation during the first complete remission with survival rates after early and late chemotherapy Intensification regimens in adult patients with acute nonlymphoblastic leukemia.

II. Determine the effect of adding immunotherapy with Corynebacterium parvum (C. parvum) on (a) bone marrow transplantation, (b) the post-Induction chemotherapy hypoplastic period, and (c) the early and late Intensification chemotherapy phase.

PROTOCOL ENTRY CRITERIA: Adult patients with acute nonlymphoblastic leukemia. FAB classification based on morphologic and cytochemical diagnosis.

PROTOCOL OUTLINE: Randomized study, following Induction and Consolidation.

Induction:

Regimen A: 3-Drug Combination Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878; VP-16213, VP-16, NSC-141540; Adriamycin, ADR, NSC-123127.

Regimen B: (Included in July 1979 version.) 2-Drug Combination Chemotherapy. Enter failures from Regimen A. m-AMSA, AMSA, NSC-249992; plus 5-Azacytidine, AZC, NSC-102816.

Consolidation:

Regimen A for 2 courses. Eligible patients proceed to first complete remission bone marrow transplantation; others proceed to early or late Intensification.

Arm IA: Bone marrow transplantation.

Arm IB: Bone marrow transplantation plus Corynebacterium parvum Burroughs-Wellcome (Coparvax), C. parvum, NSC-220537.

Arm II: Early Intensification Maintenance. 4-Drug Combination Chemotherapy plus Citrovorum factor rescue. Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; ARA-C; high-dose Methotrexate, MTX, NSC-740 with CF, NSC-3590. Patients then randomized to C. parvum.

Arm III: Late Intensification Maintenance. 3-Drug Combination Chemotherapy followed by 4-Drug Combination Chemotherapy. ARA-C; VP-16; ADR followed by CTX; VCR; ARA-C; HDMTX. Patients then randomized to C. parvum.

STRATIFICATION BY: Age, immune status, disease stage, leukemia classification.

SPECIAL STUDY PARAMETERS: Serial in vitro bone marrow culture, lymphocyte function.

END POINTS: Duration of disease-free survival; overall survival; arbitrary analysis at yearly intervals.

CURRENT STATUS: 33 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Induction:

Regimen A: ARA-C - 80 mg/sqm/day as 5-day continuous infusion; VP-16 - 60 mg/sqm/day in 5 daily 30-minute infusions; ADR - 40 mg/sqm in a single 30-minute infusion on day 6.

Regimen B: AZC - 75 mg/sqm continuous iv infusion for 5 days; AMSA - 45 mg/sqm/day iv infusion over 30 min for 3 days.

Consolidation: Repeat Induction schedule twice. Escalation is used on a sliding scale to ensure platelet counts below 100 x 10 to the ninth (and granulocytes below 2.5 x 10 to the ninth) per liter. Patients then either proceed to bone marrow transplantation or are randomized to early or late Intensification.

Arm I: Bone marrow transplantation (A) with and (B) without C. parvum - 2.5 mg/sqm iv once a week.

Arm II: CTX - 1250 mg/sqm iv (dose is increased 50 percent in both subsequent months); MTX - 0.5 mg/kg as loading dose, followed by a 24-hour infusion of MTX - 125 mg/sqm and CF-rescue - 20 mg/sqm iv every 6 hours for 12 doses; ARA-C - 250 mg/sqm iv in 4 divided doses over 24 hours; VCR - 2 mg over 24 hours. This regimen is administered monthly for a total of 6 months, 3 months of CTX and 3 months of MTX, ARA-C, and VCR. Patients are then randomized to C. parvum - 2.5 mg/sqm iv once a week.

Arm III: ARA-C, VP-16, and ADR as in Regimen A - 9 monthly infusions before proceeding to Intensification schedule as in Arm I. Patients then randomized to C. parvum - 2.5 mg/sqm iv infusion once a week.

Dosage modifications for toxicity are given.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 00330280

6.0058 BONE MARROW TRANSPLANTATION PLUS CYCLOSPORIN-A FOR ADULT ACUTE LEUKEMIA IN REMISSION

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PROTOCOL NUMBER(S) SAFR-CT-LEU-2

OBJECTIVES:

I. Compare transplantation in adult acute leukemia in first remission to early or late drug intensification.

II. Compare allogeneic bone marrow transplantation to chemotherapy in adult lymphoblastic leukemia in first remission (poor prognosis) or second remission (good prognosis).

III. Evaluate the effect of cyclosporin-A as an immunosuppressive agent on incidence and course of graft-versus-host disease (GVHD) in allografted patients.

PROTOCOL ENTRY CRITERIA: Adult patients with acute myeloblastic leukemia in first remission and adult or pediatric patients with acute lymphoblastic leukemia in first remission (with poor prognosis) or in second remission (with good prognosis).

PROTOCOL OUTLINE: Nonrandomized study.

Bone Marrow Transplantation plus Immunosuppression. Allogeneic bone marrow transplant plus Cyclosporin A.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: RIA and HPLC of plasma levels, effects on mitogenic response and MLC.

END POINTS: Response/remission, immunologic status, survival.

CURRENT STATUS: As of October 1980, 5 patients were entered.

DOSAGE SCHEDULE:

Cyclosporin A - 15 mg/kg/day for 7 days, beginning on day -1 for all patients undergoing bone marrow transplantation, then reduced to 10 mg/kg/day for 6 months, provided plasma levels and immunologic parameters are acceptable. Dosage is gradually reduced over the next 6 months, but reinstituted at original level upon evidence of recrudescence of GVHD.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 01/81

6.0059 CHEMOTHERAPY PLUS BCG IMMUNOTHERAPY WITH OR WITHOUT ALLOGENEIC TUMOR CELLS FOR ACUTE MYELOID LEUKEMIA

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PROTOCOL NUMBER(S) SWE-LCS-AML-1

OBJECTIVES:

I. Evaluate the effect of the addition of BCG immunotherapy with and without allogeneic leukemic cells to an earlier chemotherapy regimen for acute myeloid leukemia.

PROTOCOL ENTRY CRITERIA: Patients with acute myeloid leukemia.

PROTOCOL OUTLINE: Study randomized for Maintenance only.

Induction:

2-Drug Combination Chemotherapy. Daunomycin, DNR, NSC-82151 or Daunomycin-DNA complex, NSC-169533; Cytosine arabinoside, ARA-C, NSC-63878.

Maintenance:

Arm I: Immunotherapy plus 2-Drug Combination Chemotherapy. BCG-Glaxo, BCG; live allogeneic leukemic cells; DNR (or Daunomycin-DNA complex); ARA-C. Arm active 1974-1978.

Arm II: 2-Drug Combination Chemotherapy. DNR (or Daunomycin-DNA complex); ARA-C. Arm active 1974-1978.

Arm III: Immunotherapy plus 2-Drug Combination Chemotherapy. BCG; DNR (or Daunomycin-DNA complex); ARA-C. Arm active 1978.

Arm IV: Immunotherapy plus Single-agent Chemotherapy and Leucovorin Rescue. BCG; live allogeneic leukemic cells; plus (a) early Intensification with high-dose Methotrexate, MTX, NSC-740 and Citrovorum Factor, CF, NSC-3590 or (b) no early Intensification. Arm active 1978.

STRATIFICATION BY: Age; sex; classification factors: CFU, Ia-antigen, serum ferritin, initial number of blast cells; corticosteroid receptors on leukemic cells.

SPECIAL STUDY PARAMETERS: B-, T-, and null-cells; lymphocyte reactivity to leukemic cells and non-specific stimulants; colony formation and colony stimulating activity; natural killer cells; macrophage activity and frequency of septicemia in immuno- and chemotherapy; interferon levels in the serum.

END POINTS: Remission duration, survival, frequency of second remissions.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE: Not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 05/80

6.0060 COMBINATION CHEMOTHERAPY WITH ARA-C/DRB VS ARA-C/DRB-DNA COMPLEX FOR ACUTE NON-LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) SWE-LCS-780901; SWE-LCS-ANLL-1

OBJECTIVES:

I. Compare the therapeutic effect of cytosine arabinoside (ARA-C)/daunorubicin (DRB) with ARA-C/daunorubicin-DNA complex (DRB-DNA complex) in patients with acute nonlymphocytic leukemia.

PROTOCOL ENTRY CRITERIA: Patients 15 to 60 years of age with acute nonlymphocytic leukemia.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878; Daunorubicin, DRB, NSC-82151.

Arm II: 2-Drug Combination Chemotherapy. ARA-C; Daunorubicin-DNA complex, DRB-DNA complex, NSC-169533.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, survival rate, length of survival.

CURRENT STATUS: 60 patients will be entered.

DOSAGE SCHEDULE:

Arm I: ARA-C - 2 mg/kg/day iv in 2 divided doses on days 1 through 5; DRB - 1.5 mg/kg/day iv infusion on day 1.

Arm II: ARA-C as in Arm I; DRB-DNA complex - 1.5 mg/kg/day iv infusion on day 1.

All patients will be followed for 3-5 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

6.0061 INDUCTION & MAINTENANCE CHEMOTHERAPY WITH ADR/ARA-C/6-TG VS CHEMO/IMMUNOTHERAPY ADR/ARA-C/6-TG PLUS BCG IN ACUTE MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) UKM-UHW-CAR-3

OBJECTIVES:

I. Examine the effect of iv BCG on the remission and maintenance phases of acute myelogenous leukemia (AML).

II. Compare the effect of different Induction arms in patients with AML on Maintenance chemotherapy vs. chemo/immunotherapy.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with newly diagnosed AML.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I: Immunotherapy plus 3-Drug Combination Chemotherapy. BCG (Glaxo freeze-dried); Adriamycin, ADR, NSC-123127; Cytosine arabinoside, ARA-C, NSC-63878; Thioguanine, 6-TG, NSC-752.

Arm II: 3-Drug Combination Chemotherapy. ADR; ARA-C; 6-TG.

Maintenance:

Cardiff I Immunotherapy trial (Protocol No. UKM-UHW-CAR-1).

STRATIFICATION BY: Age, disease stage.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission duration, survival rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction:

Arm I: BCG - 1 ml containing 4-9 x 10 to the sixth organisms/ml iv on days 1, 14, and 29; ADR - 30 mg/sqm iv on days 6 and 7; ARA-C - 70 mg/sqm as a continuous intravenous infusion for 7 days; 6-TG - 200 mg/sqm in 2 divided doses po for 7 days.

Arm II: ADR, ARA-C, 6-TG - as in Arm I.

Maintenance:

Therapy as in Cardiff I Immunotherapy trial (Protocol No. UKM-UHW-CAR-1).

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

6C. CHRONIC LEUKEMIA

6.0062 PHASE III CHEMOTHERAPY WITH CHLORAMBUCIL FOR INDOLENT CHRONIC LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) CLB-7632

OBJECTIVES:

I. Test whether the administration of intermittent chlorambucil in patients with indolent chronic lymphocytic leukemia (CLL) of categories 2 and 3 delays or possibly prevents the development of aggressive CLL in comparison to a no-treatment group.

II. Test whether the administration of intermittent chlorambucil prolongs survival in comparison to a no-treatment group.

PROTOCOL ENTRY CRITERIA: Patients, without prior treatment, within 12 months of unequivocal diagnosis of chronic lymphocytic leukemia. Critiera for 'indolent' disease categories 2 or 3 must be satisfied; if necessary, observe patients for 12 weeks prior to study entry (Addendum 1, November 1977).

PROTOCOL OUTLINE: Randomized study.

Arm I: Control group. No treatment.

Arm II: Single-agent Chemotherapy. Chlorambucil, CLB, NSC-3088.

STRATIFICATION BY: Participating institutions, treatment phase categories 2 or 3.

SPECIAL STUDY PARAMETERS: Immunoglobulin quantitation, delayed hypersensitivity skin tests, chest X-ray.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival.

CURRENT STATUS: About 52 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Control group. No treatment, but follow and perform physical examination regularly.

Arm II: CLB - 0.5 mg/kg, po, on days 1, 29, and every 28 days thereafter. Augment dose by 0.1 mg/kg each month until the patient fulfills the following criteria for clinical improvement - reduction in size of lymph nodes and spleen, blood lymphocytes less than 20,000/microliter, neutrophils greater than 1500/microliter, platelets greater than 7500/microliter and marrow lymphocytes reduction by 33% of pretreatment values. Continue therapy until active disease or unacceptable toxicity develops.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLB - 2 mg tablets.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00271078

6.0063 PHASE III CLB/PRED CHEMOTHERAPY WITH VS WITHOUT TOTAL BODY IRRADIATION FOR PREVIOUSLY UNTREATED CHRONIC LYMPHOCYTIC LEUKEMIA

Durant, J. R., (205-934-5077) Southwestern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-79CLL348

OBJECTIVES:

I. Compare effects of intermittent chlorambucil (CLB)/prednisone (PRED) vs. intermittent CLB/PRED plus total body irradiation for previously untreated, chronic lymphocytic leukemia.

II. Determine correlation between immunologic recovery and attainment of complete remission.

PROTOCOL ENTRY CRITERIA: Patients with previously untreated chronic lymphocytic leukemia who have an absolute lymphocyte count of at least 15,000/cumm in the peripheral blood and 30% small, well-differentiated lymphocytes in the marrow. Patients must not have diabetes or fluid retention problems which could be exacerbated by PRED; hairy cell, lymphosarcoma cell, or poorly differentiated lymphocytic leukemia; Sezary's syndrome; prior chemotherapy with CLB or prior total body irradiation; second serious malignancy with expected survival of less than 2 years; more than 1 plasmapheresis; or Rai Stage 0 disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy plus Hormone Therapy. Chlorambucil, CLB, NSC-3088; plus Prednisone, PRED, NSC-10023.

Arm II: Single-agent Chemotherapy plus Hormone Therapy plus Radiotherapy. CLB; plus PRED; plus high energy (1 MeV or higher) photon total body irradiation (TBI).

STRATIFICATION: Participating institutions; Rai Stage: I and II vs. III and IV; asymptomatic vs. symptomatic disease status.

SPECIAL STUDY PARAMETERS: SMA-14, direct Coomb's test, immunoglobulins, absolute T and B cell counts, monospecific S-IG evaluation, skin tests for recall antigens.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival, survival rate.

CURRENT STATUS: 166 patients will be entered in 3.5 to 4 years.

DOSAGE SCHEDULE:

Arm I: CLB - 30 mg/sqm (escalated in increments of 4 mg/sqm q other course unless toxicity or therapeutic effect occurs) po on day 1 at bedtime with 10 mg of Compazine; PRED - 80 mg po morning after CLB on days 2 through 6. Repeat course q 2 weeks for a total of 24 courses.

Arm II: PRED - as in Arm I; TBI - 10 rad to one side of entire body (alternate side q other course) on day 1 q 4 weeks concurrent with q other course of Chemotherapy for a total of 12 courses or 120 rads.

Evaluate all patients after 12 course of Chemotherapy - continue therapy for patients with complete or partial remission for the full 24 courses. Remove from study patients without response or with disease progression. Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLB - 2 mg tablets; PRED - 5, 20 and 50 mg tablets.

DATE SUMMARIZED: 11/79

6.0064 PHASE III CHEMOTHERAPY WITH BUSULFAN (BU) VS BU/13-CIS-RETINOIC ACID FOR PREVIOUSLY TREATED CHRONIC MYELOGENOUS LEUKEMIA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama,
Birmingham, Tumor Inst., Room 225, Birmingham, Alabama,
35294, United States of America

PROTOCOL NUMBER(S) SEG-79CML358

OBJECTIVES:

I. Determine whether 13-cis retinoic acid (RA) prolongs the time development of blast crisis in patients with previously treated chronic myelogenous leukemia (CML) receiving busulfan (BU).

II. Determine whether 13-cis-RA prolongs survival in those patients.

III. Determine whether 13-cis-RA increases or decreases BU toxicity.

IV. Determine whether 13-cis-RA prolongs the duration of BU control of the chronic phase of CML.

PROTOCOL ENTRY CRITERIA: Patients over 15 years old with chronic myelocytic leukemia. Patients must have less than 10% blasts in the peripheral blood and less than 20% blasts in the bone marrow aspirate. Patients must have Philadelphia-chromosome positivity, no myelofibrosis and they must have had some prior therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Busulfan, BU, NCS-750.

Arm II: 2-Drug Combination Chemotherapy. BU; 13-cis Retinoic acid, 13-cis-RA, no NSC number given.

STRATIFICATION: Participating institutions; prior splenectomy; duration of CML: under 6 months vs. 6 to 12 months vs. 1 to 2 years vs. 2 to 3 years vs. over 3 years.

SPECIAL STUDY PARAMETERS: Bone marrow biopsy, aspirate and karyotype; leukocyte alkaline phosphatase.

END POINTS: Duration of response, toxicity/morbidity of treatment, survival time, duration of BU control.

CURRENT STATUS: 80 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BU - oral dose sufficient to induce reduction of wbc to below 15,000 and platelets to below 500,000.

Arm II: BU, as in Arm I; 13-cis-RA - 2 mg/kg day po. Evaluate patients q 28 days. Continue BU until resistance develops and 13-cis-RA for a maximum of 18 months with 8 weeks rest q 6 months. Chemotherapy other than BU may be used to control the disease. Continue treatment until development of blast crisis or death of patient.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BU - 20 mg tablets; 13-cis-RA - 10 mg capsules.

DATE SUMMARIZED: 11/79

6.0065 PHASE III CHEMOTHERAPY WITH BUSULFAN WITH OR WITHOUT VITAMIN A FOR CHRONIC MYELOGENOUS LEUKEMIA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103,
United States of America

PROTOCOL NUMBER(S) SWOG-7984

OBJECTIVES:

I. Determine the efficacy of standard-pulse, intermittent busulfan therapy plus oral vitamin A in prolonging the chronic phase of chronic myelogenous leukemia (CML), and hence in prolonging survival.

PROTOCOL ENTRY CRITERIA: Patients with newly diagnosed (less than one year) chronic stage CML as defined with respect to persistent leukocytosis, differential counting of blood leukocytes, bone marrow hypercellularity on aspiration, karyotypes Ph1 positive, and leukocyte alkaline phosphatase scores. Patients with myelofibrosis and agnogenic myeloid metaplasia must have a demonstrated Ph1 chromosome. Patients splenectomized are eligible but will be analyzed separately.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Busulfan, BU, NSC-750.

Arm II: Single-agent Chemotherapy plus Vitamin Therapy. BU; plus Vitamin A, VIT-A, NSC-122759.

STRATIFICATION BY: Age: equal to or less than 20 years vs. more than 20 years; participating institutions.

SPECIAL STUDY PARAMETERS: Bone marrow aspiration and biopsy, karyotype, liver and spleen scan, vitamin A level, leukocyte alkaline phosphatase, uric acid, SGOT, LDH, bilirubin, protime, Ca, creatinine, quantitative immunoglobulins, optional tests: skin (PPD, Mumps, Trichophyton, Candida, SK, SD); assays (terminal transferase, myeloid progenitor).

END POINTS: Toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 150 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BU - 8 mg/sqm/day po q 4 weeks. If chronic stable disease is reached (total leukocyte count of less than 50,000 but greater than 6, 000), discontinue treatment until WBC exceeds 50,000, then repeat BU. Patients with progression go off study.

Arm II: BU as in Arm I; VIT-A - 50,000 IU/day po daily for as long as patient is on study, under conditions as in Arm I. VIT-A is given daily whether or not patient is receiving BU.

All patients will be followed until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BU - 2 mg tablets; VIT-A - 50,000 IU capsules.

DATE SUMMARIZED: 10/80

6.0066 PHASE I-II CHEMOTHERAPY WITH COLCHICINE FOR REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103,
United States of America

PROTOCOL NUMBER(S) SWOG-8014

OBJECTIVES:

I. Determine the maximum dose of colchicine that may be administered on a once-weekly basis.

II. Determine the response rate (with a standard error of plus or minus 10 percent) in patients with chronic lymphocytic leukemia.

III. Determine the quantitative and qualitative toxicity of colchicine administered on a once-weekly schedule.

PROTOCOL ENTRY CRITERIA: Patients with chronic lymphocytic leukemia who have demonstrated progressive disease on studies of higher priority. Patients must have a life expectancy of at least 6 weeks, and a performance status of 0-3 (SWOG criteria). Patients must have a total bilirubin of 3 mg percent or less, and creatinine of 2.5 mg percent or less. Patients with compromised marrow are specifically eligible. Patients must have recovered from toxicities resulting from any prior therapy before initiation of treatment on this protocol.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Colchicine, NSC-757.

STRATIFICATION BY: Participating institutions; prognostic risk: good vs. fair.

SPECIAL STUDY PARAMETERS: BUN, creatinine, bilirubin, alkaline phosphatatase, SGOT, SGPT, albumin, bone marrow.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, recurrence rate.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

Colchicine - 3 mg iv push weekly (patients with bilirubin equal to or less than 1 mg percent, creatinine equal to or less than 1.5 mg percent); 2 mg iv push weekly (patients with bilirubin greater than 1 mg percent but less than 3 mg percent, creatinine greater than 1.5 mg percent but less than 2.5 mg percent). Dose is to be increased by 1 mg/week until there is evidence of biological effect, e.g., toxicity or tumor progression or regression. Treatment will be discontinued if evidence of neurologic or muscular dysfunction appears. Patients with progressive disease after 4 weeks of treatment go off study. Patients who develop unacceptable toxicity go off study. Every effort should be made to administer at least 4 weekly courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Colchicine - 0.5 mg/ml sterile solution.

DATE SUMMARIZED: 10/80

6.0067 PHASE II COMBINATION THERAPY WITH POACH (ADR/CTX/ARA-C/PRED/VCR) FOR CHRONIC LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-8025

OBJECTIVES:

I. Determine the response rate and duration of remission in patients with chronic lymphocytic leukemia treated with combination chemotherapy consisting of POACH: prednisone, vincristine, cytosine arabinoside, cyclophosphamide, and adriamycin.

II. Correlate parameters obtained in the clinical, pathological and immunological staging with response to treatment.

III. Determine the effect of stopping chemotherapy after patients have achieved a complete remission and have been given 2 Consolidation courses in order to define a cured or stabilized fraction of patients.

PROTOCOL ENTRY CRITERIA: Patients with a diagnosis of chronic lymphocytic leukemia according to the Rai classification (all stages). Patients with a monotypic expansion of a B cell clone but less than 15,000 lymphocytes/microliter or less than 40 percent marrow infiltration can be registered on Regimen A and followed for progression. Patients previously treated with a single alkylating agent and/or prednisone and patients previously treated with radiation therapy are eligible. Patients who have a well differentiated infiltrate documented in lymph nodes but no bone marrow or peripheral lymphocytosis and patients with a poorly differentiated lymphocytic infiltrate in lymph nodes or bone marrow are not eligible.

PROTOCOL OUTLINE: Nonrandomized study. Patients with chronic lymphocytic leukemia Rai Stages 0-2 enter Regimen A; those with Rai Stages 3-4 and patients with progressive disease enter Regimen B. Patients on Regimen A who develop progressive disease cross over to Regimen B.

Regimen A: Observation only.

Regimen B: 4-Drug Combination Chemotherapy plus Hormone Therapy. POACH: Prednisone, PRED, NSC-10023; Vincristine, VCR, NSC-67574; Cytosine arabinoside, ARA-C, NSC-63878; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Prior chemotherapy, prior radiotherapy.

SPECIAL STUDY PARAMETERS: CBC and platelets, Coombs' test, reticulocyte count, bone marrow aspiration and biopsy, renal and hepatic function tests, immunoglobulins, protein electrophoresis, liver and spleen scans, CAT abdomen, lymph node measurement, EKG.

END POINTS: Response/remission rate, duration of remission, duration of response.

CURRENT STATUS: At the current rate of accrual, 50-60 patients are expected to register each year.

DOSAGE SCHEDULE:

Regimen A: Patients are observed. They are evaluated monthly for the first 3 months and every 3 months thereafter. Patients who show disease progression cross over to Regimen B.

Regimen B: POACH: ADR - 15 mg/sqm iv on days 1, 8 and 15; ARA-C - 50 mg/sqm sc in 2 equally divided doses q 12 hours on days 1 through 5; CTX - 500 mg/sqm iv on day 1; VCR - 2 mg iv on day 1; PRED - 100 mg po on days 1 through 7. Course is repeated q 28 days. In the absence of severe myelosuppression, the dose levels of ADR, ARA-C, and CTX will be increased by 25 percent. Patients with evidence of disease progression after 2 courses of treatment go off study. Responders receive 4 more courses of POACH for a total of 6 courses. Patients with CR after 6 courses receive 2 more courses; those with PR or clinical improvement receive 4 more courses of POACH. Patients who convert to CR after 10 courses receive 2 courses of COAP: ARA-C/VCR/CTX/PRED and then go off study. ADR is continued only at the discretion of the primary investigator after 10 courses of POACH (a total dose of 450 mg/sqm of ADR). Responders continue to receive COAP until CR or evidence of disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100 and 500 mg vials; PRED - 5, 20, and 50 mg tablets; VCR - 1 and 5 mg ampules.

DATE SUMMARIZED: 12/80

6.0068 STAGING AND MULTIMODAL THERAPY FOR CHRONIC LYMPHOCYTIC LEUKEMIA USING CTX/ADR/VCR/ARA-C/PRED AND THYMOSIN

Murphy, S., (713-792-2121) University of Texas, M. D. Anderson Hospital & Tumor Institute, Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-363; MDA-DT-7971

OBJECTIVES:

I. Determine the complete and partial response to a combination chemotherapy consisting of cyclophosphamide (CTX), adriamycin (ADR), vincristine (VCR), cytosine arabinoside (ARA-C), and prednisone (PRED).

II. Determine the effect of treatment with the immunorestorative, biological response modifier thymosin, and to determine if it increases the number and function of T lymphocytes and host defense parameters in those patients who obtain complete remission.

III. Compare patients defined as responders by clinical criteria with the immunological criteria for complete remission (i.e., return to normal T and B lymphocyte differential in blood and bone marrow).

IV. Correlate parameters of clinical staging, pathological staging, and immunological staging with the immunological characterizations of the malignant and non-malignant cell population, both pre- and post-therapy.

PROTOCOL ENTRY CRITERIA: Patients with monotypic expansion of lymphoid cells morphologically consistent with CLL (small lymphocytes) of B, T, or null cell type are eligible.

PROTOCOL OUTLINE: Patients achieving complete remission on Regimen A are randomized to Arms I and II.

Regimen A: 4-Drug Combination Chemotherapy plus Hormone Therapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Cytosine arabinoside, ARA-C, NSC-63878; and Prednisone, PRED, NSC-10023.

Arm I: Immunoreconstitution. Thymosin.

Arm II: No further therapy.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: None given.

CURRENT STATUS: Approximately 4 years will be required to accrue 60 patients in each treatment link.

DOSAGE SCHEDULE:

Regimen A: ADR - 15 mg/sqm, iv, days 1, 8, and 15; CTX - 500 micrograms/sqm, iv, day 1; VCR - 2 mg, iv, day 1; ARA-C - 25 micrograms/sqm, sc, q 12 hrs, days 1-5; PRED - 100 mg, po, days 1-7. Patients achieving complete remission are randomized to Arms I and II.

Arm I: Immunoreconstitution with Thymosin. No details given.

Arm II: No further therapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

6.0069 COMBINATION CHEMOTHERAPY WITH ARA-C/RBD/VCR PLUS HORMONE THERAPY WITH PREDNISONE FOR ADULTS UNDER AGE 50 WITH CHRONIC MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) MDAR-367; MDA-DT-7978

OBJECTIVES:

I. Increase the response rate and prolong remission duration in patients under the age of 50 with CML.

II. Use a chemotherapy program (ROAP) incorporating maximum tolerated doses of rubidazone (RBD), cytosine arabinoside (ARA-C), vincristine (VCR) and prednisone (PRED).

III. Determine what cytogenetic changes occur during a course of chemotherapy plus hormone therapy and whether they correlate with response rate and duration of remission.

IV. Store both peripheral blood and bone marrow at the point of maximum reduction of the Philadelphia chromosome for autologous bone marrow transplantation in the blastic transformation of the disease.

PROTOCOL ENTRY CRITERIA: Patients less than 50 years of age with a diagnosis of CML will be eligible for all stages of protocol.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. Cytosine arabinoside, ARA-C, NSC-63878; Vincristine, VCR, NSC-67574; Rubidazone, RBD, NSC-164011; plus Prednisone, PRED, NSC-10023.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response.

CURRENT STATUS: Approximately 25 patients per year will be entered.

DOSAGE SCHEDULE:

RBD - 300 mg/sqm iv infusion on day 1; ARA-C - 80 mg/sqm/day for 10 days; VCR - 2 mg iv infusion on day 1; PRED - 100 mg po daily for 5 days. Additional courses: RBD and VCR on day 1; ARA-C days 1 through 10; PRED days 1 through 5.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

6.0070 CHEMOTHERAPY WITH VM-26 AND AMSA IN COMBINATION OR AS SINGLE AGENTS FOR CHRONIC LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) MDAR-422; MDA-DT-8042

OBJECTIVES:

I. Evaluate the efficacy of VM-26 and m-AMSA as single agents and in combination in inducing remission in patients with refractory chronic lymphocytic leukemia (CLL).

II. Determine the duration of remission in responding patients.

III. Determine whether combination chemotherapy will prolong the survival of patients with refractory CLL.

IV. Determine the toxicity related to this chemotherapeutic regimen.

PROTOCOL ENTRY CRITERIA: Patients with a diagnosis of chronic lymphocytic leukemia who have failed higher priority protocols MDA-DT 74-10 and MDA-DT 79-71 or other combination chemotherapeutic regimens. Patients previously treated with single-agent therapy (e.g., chlorambucil or steroids or any drug included in this protocol) are not eligible. Patients with a lymph node diagnosis of WDLL are not eligible; those with a diagnosis of lymphosarcoma cell leukemia are eligible but will be evaluated separately. Patients must have been off all treatment for a minimum of 4 weeks at time of entry.

PROTOCOL OUTLINE: Randomized study. Failures on Arm II proceed to Regimen A.

Arm I: 2-Drug Combination Chemotherapy. VM-26, NSC-122819; m-AMSA, AMSA, NSC-249992.

Arm II: Single-agent Chemotherapy. VM-26.

Regimen A: Single-agent Chemotherapy. AMSA.

STRATIFICATION BY: Chronic lymphocytic leukemia vs. lymphosarcoma cell leukemia.

SPECIAL STUDY PARAMETERS: Hematologic function tests.

END POINTS: Response/remission rate, duration of remission, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 25 evaluable patients for each arm is required.

DOSAGE SCHEDULE:

Arm I: VM-26 - 100 mg/sqm iv on days 1 and 2; AMSA - 20 mg/sqm iv on days 1, 2, and 3 q 28 days. Responders after 2 courses receive 4 more courses; failures go off study. After 6 courses, patients in CR are taken off treatment and are observed. Patients in PR continue treatment until CR.

Arm II: VM-26 - 100 mg/sqm iv on days 1 and 2 q 28 days. Responders after 2 courses receive 4 more courses; failures proceed to Regimen A. Patients in CR after 6 courses are taken off treatment and observed. Patients in PR continue treatment until CR.

Regimen A: AMSA - 30 mg/sqm iv on days 1, 2, and 3 q 28 days. Responders after 2 courses receive 4 more courses; failures go off study. Patients in CR after 6 courses stop treatment and are observed. Those with PR continue on AMSA until CR.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/80

6.0071 COMBINATION CHEMOTHERAPY WITH VCR/BCNU/CTX/L-PAM/PREDNISONE FOR CHRONIC LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) MSKCC-747

OBJECTIVES:

I. Gain better knowledge of pathophysiology and natural history of chronic lymphocytic leukemia.

II. Obtain longer objective and subjective remissions and achieve better treatment for the accelerated stage of chronic lymphocytic leukemia.

PROTOCOL ENTRY CRITERIA: Patients with chronic lymphocytic leukemia, SK Stages 0-IV, with persistent peripheral lymphocytes of more than 15,000/cumm, and bone marrow lymphocytosis greater than 50%.

PROTOCOL OUTLINE: Nonrandomized study.

Enter patients by stage and age: Stage 0 and I patients to Regimen A; Stage II patients over the age of 60 to Regimen B; Stage II patients below 60 and Stage III and IV patients to Regimen C.

Regimen A: Conventional management only.

Regimen B: Follow-up and observation only.

Regimen C: 4-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; BCNU, NSC-409962; Cyclophosphamide, CTX, NSC-26271; Melphalan, L-PAM, NSC-8806; Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Serum complement, skin testing for delayed sensitivity, scanning electron microscope studies of lymphocytes, cell surface markers, serum cryoglobulin and antigen-antibody complexes, red cell survival and splenic sequestration studies (for patients with evidence of hemolysis), flash H-3-thymidine labeling index and mitotic index of marrow and blood lymphocytes.

END POINTS: Response/remission rate, duration of response, disease-free interval, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Not applicable.

Regimen B: Not applicable.

Regimen C: VCR - 1 mg/sqm iv on day 1; BCNU - 0.5 mg/kg iv on day 1; CTX - 10 mg/kg iv on day 1; L-PAM - 0.25 mg/kg po on days 1 through 4; PRED - 1 mg/kg po on days 1 through 7 - reduce to 0.5 on day 7. Discontinue PRED on day 14 or maintain patients in poor condition on smaller doses. Repeat course on day 35. Continue indefinitely for responders. Alternative combination given for patients unable to tolerate above regimen.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/77

6.0072 PHASE III BUSULFAN (BU) INDUCTION CHEMOTHERAPY FOLLOWED BY BU/LEVAMISOLE MAINTENANCE VS BU ALONE FOR GOOD-RISK CML

Haanen, C., (Netherlands 080-514762) European Org. for Research on Treatment of Cancer, Leukemia and Hematosarcoma Cooperative Group, University of Nijmegen, Geert Grooteplein Zuid 10, 6525 GA Nijmegen, The Netherlands
PROTOCOL NUMBER(S) EORTC-06771

OBJECTIVES:

I. Assess effectiveness of levamisole as adjuvant in Phase III trial to busulfan treatment on onset metamorphosis of Phl-positive CML and on overall survival time.

II. Assess prognostic factors in Phl-positive chronic myeloid leukemia.

III. Accurately assess the alternative forms of metamorphosis.

PROTOCOL ENTRY CRITERIA: Patients with chronic myelogenous leukemia 15 to 65 years of age with Philadelphia (Phl) chromosome and immature, white blood cells above 80,000/sqm (or approaching that number) in the circulating blood. Patients must not have been treated with busulfan, hydroxyurea or other cytoreductive drugs for more than 3 months, and must have platelet counts between 100,000 and 450,000 cumm. Enter patients with platelet counts outside these limits or those that are otherwise poor risks to protocol EORTC-06772.

PROTOCOL OUTLINE: Randomized study for Maintenance only.

Induction: Single-agent Chemotherapy. Busulfan, BU, NSC-750.

Maintenance: Randomize responders from Induction to Arm I or Arm II.

Arm I: Single-agent Chemotherapy plus Immunotherapy. BU; Levamisole, LEV, NSC-177023.

Arm II: Single-agent Chemotherapy. BU.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Bone marrow aspiration, bone marrow biopsy; cytogenetic studies; LDH.

END POINTS: Response/remission rate; survival rate; survival time; recurrence rate; time to metamorphosis; type of metamorphosis or blastic crisis.

—CURRENT STATUS: 152 patients will be entered to Maintenance.

DOSAGE SCHEDULE:

Enter patients with wbc above 80,000, or below if wbc are increasing 20,000/2 months.

Induction: BU - 3 mg/sqm/day (route not given). Increase to 4 mg/sqm/day in 4 weeks if response is inadequate. Discontinue BU as soon as wbc count is less than 30,000/cumm; blast cells are less than 5%; and platelet count is between 100,000 and 400,000/cumm. Nonresponders go off study; responders are randomized for Maintenance.

Arm I: BU - adjust dosage individually from 0 to 2 mg/sqm/day for 1 to 7 days q week maintaining wbc at less than 30,000/cumm. Increase dose of BU (as wbc increases) to 4 to 6 mg/sqm/day; LEV - 100 mg/sqm po q 7 days (preferably Monday with last meal). Continue therapy with LEV when BU is temporarily interrupted. Discontinue LEV if a granulocytosis occurs.

Arm II: BU as in Arm I.

Continue to follow all patients every 3 months until appearance of metamorphosis or until death.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: LEV - 50 mg tablets. .

DATE SUMMARIZED: 05/79

6.0073 CHEMOTHERAPY WITH CHLORAMBUCIL FOR CHRONIC LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) EORTC-5

OBJECTIVES:

I. Compare disease progression in slowly proliferating chronic lymphocytic leukemia when treated with chlorambucil chemotherapy vs. no treatment.

PROTOCOL ENTRY CRITERIA: Patients with stable chronic lymphocytic leukemia with an absolute lymphocyte count of at least 5000/cumm and a minimum of 50 lymphocytic elements in the bone marrow myelogram. Patients with or without adenopathy and with or without splenomegaly are eligible. Observe patients for a period of time to exclude other diseases. Patients should have had slowly proliferating disease for at least 6 to 10 months.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Chlorambucil, CLB, NSC-3088.

Arm II: Controls. No therapy.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Blood and urine electrophoresis, immunoelectrophoresis, Paul-Bunnell test, immunological survey.

END POINTS: Response rate, toxicity/morbidity of treatment, survival rate, duration of survival, changes in lymphocyte and bone marrow status, tumor incidence.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Initial therapy. CLB - 3 mg/sqm frequency not given, maximum dose 15 mg/day) given over a period of 3 months. Escalate or reduce dosage according to the lymphocyte count, which should be kept below 10,000 or 15,000 depending on the initial count.

Maintenance: Continue therapy to maintain the results achieved by the initial therapy.

Evaluate patients monthly in the early months, then q 2 months for 1 year and at least q 6 months thereafter.

Arm II: No treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

6.0074 CHEMOTHERAPY WITH CLB VS COP (VCR/CTX/PRED) VS CHOP (VCR/CTX/PRED/ADR) FOR CHRONIC LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) FRE-LLC-80

OBJECTIVES:

I. Evaluate treatment of CLL within 3 prognostic groups: Group A, most favorable prognosis (no treatment vs. chlorambucil); Group B, intermediate prognosis (chlorambucil vs. vincristine/cyclophosphamide/prednisone); and Group C, poor prognosis (vincristine/cyclophosphamide/prednisone, with and without adriamycin).

PROTOCOL ENTRY CRITERIA: Patients under 80 years of age with previously untreated CLL and a lymphocyte count meeting protocol specifications. Patients must present no other disease. Group B and C patients may not be allergic to corticoids, nor Group C patients to adriablastine.

PROTOCOL OUTLINE: Randomized study. Group A (good prognosis) patients are randomized to Arm I or Arm II, Group B (intermediate prognosis) patients to Arm II or Arm III, and Group C (poor prognosis) patients to Arm III or Arm IV.

Arm I: No treatment.

Arm II: Single-agent Chemotherapy. Chlorambucil, CLB, NSC-3088.

Arm III: 2-Drug Combination Chemotherapy plus Hormone Therapy. COP: Vincristine (Oncovin), VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; Prednisone, PRED, NSC-10023.

Arm IV: 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: CTX; VCR; PRED; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hemogram, myelogram, bone marrow biopsy, thorax x-ray, lymphography, Coombs' test.

END POINTS: Survival time, response/remission rate.

CURRENT STATUS: 850 patients will be entered in 8-9 years.

DOSAGE SCHEDULE:

Arm I: Observation only.

Arm II: CLB - 0.1 mg/kg po, indefinitely.

Arm III: COP: VCR - 1 mg/sqm on day 1 by perfusion; CTX - 300 mg/sqm po on days 1 to 5; PRED - 40 mg/sqm po on days 1 to 5, decreasing subsequently by half doses. Continue COP q 4 weeks for 6 months, then q 3 months for 18 months.

Arm IV: COP as in Arm III plus ADR - 25 mg/sqm on day 1.

Patients are evaluated at 9 months; those showing disease progression into another group cross over to appropriate arm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

6.0075 CHEMOTHERAPY WITH AZACYTIDINE/VP-16 FOR BLAST CRISIS OF CHRONIC MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) URU-LEU-7801; BCRP-7812

OBJECTIVES:

I. Determine the activity of azacytidine (AZC)/VP-16 against blast crisis or accelerated phase of chronic myelogenous leukemia.

PROTOCOL ENTRY CRITERIA: Patients with over 50% bone marrow blasts and progranulocytes and/or over 30% peripheral blood blasts and progranulocytes. Patients must have no chemotherapy within 2 weeks of entry, no prior exposure to the study agents and no splenic or spray irradiation during therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction and Maintenance: 2-Drug Combination Chemotherapy. Azacytidine, AZC, NSC-102816; VP-16, NSC-141540.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Chromosome analysis, spinal tap.

END POINTS: Response/remission rate, disease-free interval.

CURRENT STATUS: A minimum of 20 patients will be entered.

DOSAGE SCHEDULE:

Induction: AZC - 150 mg/sqm iv in 3 divided doses (increase by 50 mg/sqm/day each course if toxicity is not severe) on days 1 through 5; VP-16 - 75 mg/sqm iv infusion (increase by 25 mg/sqm/day each course if toxicity is not severe) on days 1 through 5. If peripheral count remains 5,000 or above, repeat course on day 14 or repeat with escalated doses when marrow is 2 to 4 plus and contains 40% or more blasts. Give a maximum of 3 courses. Remove from study patients with disease progression after 2 courses.

Maintenance: Enter patients with M1 or M2 marrow after Induction when toxicity has abated. AZC - 100 mg/sqm iv in 3 divided doses on days 1 through 5; VP-16 - 50 mg/sqm iv on days 1 through 5. Repeat course q 8 weeks. Continue Maintenance until patients decline to M3 marrow or extramedullary disease (other than CNS relapse) occurs. Give Cranial Radiotherapy to patients with blasts over 200, 000/cumm - 300 rads to the brain for 2 days.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZC - 100 mg vials; VP-16 - 100 mg vials.

DATE SUMMARIZED: 12/78

6D. LEUKEMIA—GENERAL

6.0076 PHASE II HORMONE THERAPY WITH PREDNIMUSTINE FOR REFRACTORY ACUTE LEUKEMIA IN CHILDREN

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PROTOCOL NUMBER(S) CCG-083

OBJECTIVES:

I. Determine the therapeutic efficacy and toxicity of prednimustine in children with refractory leukemia.

PROTOCOL ENTRY CRITERIA: Patients under 18 years old with recurrent acute leukemia resistant to all conventional chemotherapy. Patients must have adequate hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Hormone Therapy. Prednimustine, NSC-134087.

STRATIFICATION BY: Participating institutions; disease type: acute lymphocytic leukemia vs. acute non-lymphocytic leukemia.

SPECIAL STUDY PARAMETERS: Hepatic function.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of response.

CURRENT STATUS: As of 10/80, 118 patients have been entered.

DOSAGE SCHEDULE:

Prednimustine - 40 mg/sqm po daily. Continue for 8 weeks, then evaluate. Continue complete responders at 20 mg/sqm (escalating at relapse) po daily. Remove patients when disease progresses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

6.0077 PHASE I-II PILOT CHEMOTHERAPY WITH M-AMSA FOR REFRACTORY ACUTE LEUKEMIA

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PROTOCOL NUMBER(S) SEG-RAL-P38R

OBJECTIVES:

I. Determine the activity of m-AMSA in the treatment of refractory acute leukemia.

PROTOCOL ENTRY CRITERIA: Patients with acute granulocytic leukemia (acute myeloblastic, acute monocytic, acute myelomonocytic leukemias), erythroleukemia, blast crisis of chronic granulocytic leukemia and acute lymphoblastic leukemia refractory to standard therapy or primary treatment protocols. Patients should have recovered from hematologic effects of prior chemotherapy, should have a Karnofsky performance status of at least 40%, and should have an estimated survival of at least one month.

PROTOCOL OUTLINE:

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 14 to 25 patients will be entered.

DOSAGE SCHEDULE:

Induction.

Enter cohorts of 3 patients. AMSA - 50 mg/sqm/day iv 1 hr infusion on days 1 through 5. If marrow is more than 30% cellular with more than 30% abnormal cells repeat course on day 15. Delay further therapy if marrow is hypocellular and there is a decrease in the number of blasts. If there are not therapeutic effects and toxicity is acceptable escalate dosage by 10/mg/sqm in each subsequent cohort of 3 patients. When response and toxicity occur, treat 6 patients at that dose level. Then convert to a Phase II study.

(Phase II Regimen for Induction added March 1979. AMSA - 90 mg/sqm iv in 2-hour infusion in 300 ml 5 percent DW daily for 5 days. (If total bilirubin exceeds 2 mg/dl, reduce dose by 25 percent). Repeat courses will be considered on day 15. Bone marrow aspirate and biopsy to be done before each course unless there are more than 1000 cubic millimeters of circulating blasts. If marrow greater than 50 percent and abnormal cells exceed 30 percent, repeat course on day 15. Hypocellular marrow (less than 50 percent) and blasts decreased from pre-treatment marrow will delay further treatment and repeat marrow done in 4-7 days. If regrowth of leukemic cells is apparent, another course of AMSA is indicated. If after 8 weeks of treatment complete remission is not obtained, patients will be treated on a subsequent group protocol for refractory leukemia or at physician's discretion.)

Maintenance.

Enter complete responders. AMSA - 150 mg/sqm single dose iv q 21 days until relapse.

(Phase II Regimen for Maintenance added March 1979. AMSA - 150 mg/sqm iv 1-2 hour infusion in 300 ml 5 percent DW once every 3 weeks. Weekly blood counts will be obtained and a repeated dose will be considered every 3 weeks if blood counts permit. Treatment will be delayed until granulocytes recover to more than 1500 and/or platelets more than 100,000. If re-treatment is delayed more than 2 weeks, a repeat bone marrow to assess leukemia status is suggested. Maintenance therapy will be continued until relapse.)

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules or vials.

DATE SUMMARIZED: 04/80

6.0078 PHASE II STUDY OF THE EFFECT OF DOSAGE SCHEDULE ON ACTIVITY OF AZACYTIDINE FOR ACUTE LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-7603; MDAR-126

OBJECTIVES:

I. Compare the activity and toxicity of single-day infusion of 5-azacytidine vs. intermittent infusion given over 5 days.

PROTOCOL ENTRY CRITERIA: Patients with progressive acute leukemia unresponsive to higher priority protocols, with at least 30% leukemic cells and at least 30% bone marrow cellularity.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Azacytidine, AZC, NSC-103816, single-day infusion. (Amended to continuous 10-day infusion, February 1977).

Arm II: Single-agent Chemotherapy. AZC, intermittent 5-day infusion. (Arm deleted, February 1978).

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Weekly SMA-100.

END POINTS: Remission/response rate; duration of response; duration of survival; toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: AZC - 750 mg/sqm given in 3 divided doses over 2 hours each at 4-hour intervals on day 1 only. Changed to AZC - 150 mg/sqm/day iv infusion for 10 days, February 1978.

Arm II: AZC - 300 mg/sqm/day iv given in 4 divided doses over 4 hours of each 6-hour period daily for 5 days. Schedule changes: AZC -300 mg/sqm/day iv as a continuous infusion for 5 days (Amendment 1, May 1976), then AZC - 200 mg/sqm/day iv as a continuous infusion for 5 days (Amendment 2, December 1976). Arm deleted in February 1978.

Repeat course of Arm I and Arm II q 3 weeks unless bone marrow cellularity remains less than 10% or there is evidence of progression - at least 50% increase in bone marrow disease. Adjust dosages to maintain neutrophil counts not below 1000/cumm and platelet counts not below 50,000/cumm. Maintain complete responders on therapy given q 4 weeks until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZC - 50 mg vials.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00920278

6.0079 PHASE III VAC INDUCTION, MAINTENANCE WITH ARA-C/TG ALTERNATING WITH MINI-COAP, AND VAC REINFORCEMENT FOR AML/ALL IN CHILDREN

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PROTOCOL NUMBER(S) SWOG-7721; MDAR-246

OBJECTIVES: (This protocol replaces SWOG-7637 and was replaced by SWOG 7834).

I. Evaluate a remission induction program with VAC: vincristine (VCR)/adriamycin (ADR)/prednisone (PRED) in previously untreated acute non-lymphocytic leukemia or acute lymphocytic leukemia in first relapse.

II. Evaluate a Maintenance regimen with cytosine arabinoside (ARA-C) plus thioguanine (TG) alternating with mini-COAP: VCR/ARA-C/cyclophosphamide (CTX)/PRED and also the effects of periodic reinforcement with VAC.

III. Investigate the effects on development of CNS leukemia and the effects on prolongation of remission maintenance by the addition of CNS prophylaxis.

IV. Evaluate the outcome by histologic subgroups in response to therapy.

PROTOCOL ENTRY CRITERIA: Previously untreated patients under 21 years of age with acute myelocytic, acute myelomonocytic leukemia, or acute lymphocytic leukemia in first relapse, who may have CNS disease. Chronic granulocytic leukemia in blastic crisis, erythroleukemia and other rare forms of myelocytic leukemias are eligible but will be entered separately.

PROTOCOL OUTLINE: Randomized study. Enter all patients to Induction Regimen A, then randomize M1 responders to Arms I and II, nonresponders go to Regimen B. Enter all patients exiting from alternate Induction Regimen B to Maintenance Arm I, all patients with chronic granulocytic leukemia in blastic crisis, erythroleukemia or other rare forms of myelocytic leukemia to Maintenance Arm II. Treat patients free of CNS disease at entry with triple therapy with Maintenance as in CNS #5 (SWOG-7308); if CNS disease present, enroll patients simultaneously in CNS #6 program (Addendum, June 1978).

Induction:

Regimen A: 2-Drug Combination Chemotherapy plus Hormone Therapy. VAP: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Prednisone, PRED, NSC-10023.

Regimen B: 2-Drug Combination Chemotherapy. Thioguanine, TG, NSC-752; Cytosine arabinoside, ARA-C, NSC-63878.

Maintenance:

Arm I: 2-Drug Combination Chemotherapy alternating with 3-Drug Combination Chemotherapy plus Hormone Therapy. ARA-C; TG; alternating with mini-COAP: VCR; ARA-C; Cyclophosphamide, CTX, NSC-26271; PRED.

Arm II: 2-Drug Combination Chemotherapy alternating with 3-Drug Combination Chemotherapy plus Hormone Therapy plus 3-Drug Combination Chemotherapy plus Hormone Therapy Reinforcement. ARA-C; TG; alternating with mini-COAP as in Arm I, plus VAP, as in Induction Regimen A.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Karyotype for Philadelphia chromosome, cytochemical stain and electron microscopy of bone marrow, fetal hemoglobin, IVP and skeletal survey (Revision April 1979).

END POINTS: Response/remission rate, remission duration.

CURRENT STATUS: 30 patients per year will be entered in about 3 years.

DOSAGE SCHEDULE:

Regimen A: VAP: VCR - 2.0 mg/sqm (maximum dose 2 mg) iv on days 1, 8 and 15; ADR - 30 mg/sqm (maximum total dose 450 mg/sqm) iv on days 1, 2 and 3; PRED - 60 mg/sqm/day (maximum dose 60 mg) po in 3 divided doses. Repeat course on day 21 or 28 for M1 or M2 responders. If M3 on day 22, enter patients to Regimen B.

Regimen B: AT: TG - 100 mg/sqm po followed in 12 hours by ARA-C -100 mg/sqm sc. Repeat course q day for 5 days. Repeat 5-day course q 15 days until bone marrow cellularity is 10% or less. If bone marrow still M3 after 3 courses or if disease is progressive, remove patient from study.

Maintenance: Randomize M1 responders with an absolute granulocyte count of at least 1000 from Induction Regimen A to Arm I or II. Enter responders exiting from Regimen B to Arm II.

Arm I: Begin on day 43. ARA-C, TG as in Regimen B given for 4 doses. On day 64, begin mimi-COAP: VCR - 2.0 mg/sqm iv on day 1; ARA-C - 105 mg/sqm/day iv given in 3 divided doses q 8 hours on days 1, 2, 3 and 4; CTX and PRED - 105 mg/sqm/day each given iv same schedule as ARA-C. Give alternate courses q 21 days.

Arm II: Give 4 Maintenance courses (2 each AT, Mini-COAP) as in Arm I, then initiate reinforcement with VAP: as in Regimen A. Taper PRED to discontinue by day 28 of course. Repeat entire sequence q 12 weeks, until maximum ADR has been given, then discontinue reinforcement course.

Remove from study patients with M3 bone marrow or 2 separate M2 marrow with at least 50% cellularity at 3-week interval.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: PRED - 5 mg tablets; VCR - 1 and 5 mg vials; MTX - 20 and 50 mg vials; CTX - 100, 200 and 500 mg vials; ARA-C - 100 mg vials; ADR - 10 mg vials; TG - 40 mg tablets.

DATE SUMMARIZED: 07/79

PATIENT ACCRUAL: 00421178

6.0080 PHASE II CHEMOTHERAPY WITH RUBIDAZONE FOR CHILDREN WITH REFRACTORY ACUTE LYMPHOBLASTIC OR ACUTE MYELOGENOUS LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-7818; MDAR-313

OBJECTIVES:

I. Determine the clinical efficacy of rubidazone (RBD) in the induction of remission in children with acute leukemia in relapse.

II. Determine the toxicity of RBD in children with acute leukemia in relapse.

III. Determine and compare the response rate to a higher and a lower dose of RBD given as a single injection. (Amendment 1, August 1979).

IV. Determine whether there is any cross-resistance between adriamycin & RBD (Amendment 1).

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age in M3 bone marrow relapse of acute lymphoblastic or myelogenous leukemia, including acute stem cell, undifferentiated, monomyelocytic, monocytic, promyelocytic, or erythroleukemia. Patients must be ineligible for higher priority protocols or resistant to standard induction agents, including vincristine and prednisone. Patients must have adequate cardiac function and an expected survival of at least 6 weeks; they must have had no prior therapy for 1 week and must have recovered from any toxicity. They must have previously received no more than 200 mg/sqm of adriamycin or daunomycin (Amendment 1).

PROTOCOL OUTLINE: Randomized study (as of Amendment 1, August 1979).

Arm I: Single-agent Chemotherapy. Rubidazone, RBD, NSC-164011, higher dosage; plus pretreatment with Benadryl, NSC-33299; and supportive therapy with Allopurinol, NSC-1390.

Arm II: Single-agent Chemotherapy. RBD, lower dosage; plus Benadryl and Allopurinol as in Arm I.

STRATIFICATION BY: Participating institutions, number of prior relapses, resistance to adriamycin (Amendment 1).

SPECIAL STUDY PARAMETERS: Echocardiogram.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 50 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: RBD - 450 mg/sqm iv infusion over 1 hour.

Arm II: RBD - 300 mg/sqm iv infusion over 1 hour. Premedicate patients (in Arm I and Arm II) with Benadryl - 1 mg/kg iv. Also give Allopurinol - 200 mg/sqm/day in 2 to 3 divided doses for 1 week.

Examine bone marrow on day 28. Remove complete responders from study. Repeat course for partial responders with M2 or M3 bone marrow.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/79

PATIENT ACCRUAL: 00260879

6.0081 PHASE II ROAP (RBD/VCR/ARA-C/PRED) VS ADOAP (ADR/VCR/ARA-C/PRED) WITH INTENSIFICATION AND/OR IMMUNOTHERAPY FOR ACUTE LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-7823/24/25/26

OBJECTIVES: (This study replaces SWOG-7626 A&B, SWOG-7763, SWOG-7762 and Maintenance of SWOG-7717).

I. Compare the efficacy of the 4-drug combination chemotherapy regimen, ROAP: rubidazone (RBD)/vincristine (VCR)/cytosine arabinoside (ARA-C)/prednisone (PRED) to ADOAP (the same combination using adriamycin (ADR) in place of RBD) in adult acute leukemia, as determined by remission rate, remission duration and survival.

II. Determine the comparative toxicity of these regimens.

III. Determine whether late intensification therapy at 9 months after complete remission will improve long-term, disease-free survival.

IV. Determine whether immunotherapy using levamisole for 6 months after 12 months of complete remission on chemotherapy improves disease-free survival.

V. Determine the effects of intrathecal ARA-C on the incidence of CNS leukemia.

VI. Determine reproducibility of the FAB/histologic classification and correlation to response to therapy in 200 consecutive cases of acute leukemia.

VII. Study the effects of intensive supportive care in the management of acute leukemia.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with acute leukemia diagnosed by bone marrow smear, clot section, and/or biopsy. Patients must have an absolute infiltrate of 50% or more leukemic cells, if less, evidence of disease progression is required. Patients must have adequate renal and hepatic function and may have undergone no more than one course of prior chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Induction and Consolidation (SWOG-7823).

Arm I: 4-Drug Combination Chemotherapy. ROAP: Rubidazone, RBD, NSC-164011; Vincristine, VCR, NSC-67574; Cytosine arabinoside, ARA-C, NSC-63878; Prednisone, PRED, NSC-10023.

Arm II: 4-Drug Combination Chemothrapy. ADOAP: Adriamycin, ADR, NSC-123127; VCR, ARA-C, PRED.

CNS Prophylaxis (SWOG-7824): Separately rerandomize patients in Arms I or II to Arms III or IV.

Arm III: Lumbar Puncture plus Single-agent Intrathecal Chemotherapy. ARA-C.

Arm IV: No diagnostic lumbar puncture.

Maintenance (SWOG-7823).

Arm V: 3-Drug Combination Chemotherapy. OAP: VCR, ARA-C, PRED.

Late Intensification (SWOG-7825). Rerandomize patients to Arms VI or VII.

Arm VI: 3-Drug Combination Chemotherapy - OAP (continued Maintenance).

Arm VII: 4-Drug Combination Chemotherapy. POMP: PRED; VCR; Methotrexate, MTX, NSC-740; 6-Mercaptopurine, 6-MP, NSC-755.

Rerandomize patients after 12 months in CR.

Late Maintenance.

Arm VIII: Single-agent Immunotherapy. Levamisole, LEV, NSC-177023.

Arm IX: No treatment.

STRATIFICATION BY: Participating institutions; SWOG-7823: age - 50 or more vs. less than 50 years old; SWOG's 7824 and 7825: age and induction therapy; SWOG-7826: age, induction therapy and late intensification treatment.

SPECIAL STUDY PARAMETERS: Hepatic, renal, bone marrow function, HBSA, FAB classification, CSF studies.

END POINTS: Response/remission rate, duration of remission, length of survival, disease free interval, toxicity/morbidity of treatment.

CURRENT STATUS: 666 patients will be entered in nearly 3 1/2 years.

DOSAGE SCHEDULE:

Induction and Consolidation (SWOG-7823).

Arm I: ROAP: RBD - 200 mg/sqm iv on day 1; VCR - 2 mg iv on day 1; ARA-C - 70 mg/sqm iv on days 1 through 7; PRED - 100 mg po on days 1 through 5. Evaluate patients on days 7 or 8. Give patients in complete remission (CR) 3 additional courses of ROAP, then randomize patients to Arm III or IV and enter to Consolidation: RBD - 150 mg/sqm iv on day 1; ARA-C - 100 mg/sqm iv on days 1 through 5; VCR - 1.5 mg/sqm (maximum dose 2 mg/sqm) iv on day 1; PRED - 100 mg po on days 1 through 5. Repeat for 2 additional courses of Consolidation upon hematological recovery. Give patients with progressive disease after the first Induction course: ARA-C - 70 mg/sqm iv on days 10 through 14, then enter to reinduction, if disease is still progressive. Remove patients not achieving complete remission after 3 Induction courses from study.

Arm II: ADOAP: ADR - 40 mg/sqm iv on day 1; VCR, ARA-C, PRED and subsequent therapy and rerandomization as in Arm I, substituting ADR for RBD in Reinduction and Consolidation courses. Reduce ADR to 30 mg/sqm on day 1 for Consolidation courses.

CNS Prophylaxis (SWOG-7824).

Arm III: Perform diagnostic lumbar puncture. If no CNS leukemia is found, give ARA-C - 30 mg/sqm it q 7 days for 8 weeks.

Arm IV: No lumbar puncture.

Remove from study any patient with CNS or meningeal leukemia at any time during study.

Maintenance (SWOG-7823).

Arm V: Enter all patients in complete remission following 3 courses of Consolidation. OAP: ARA-C - 100 mg/sqm sc in 3 divided doses on days 1 through 5; VCR - 1 mg iv on day 1; PRED - 100 mg po on days 1 through 5. Repeat q month or until relapse which disqualifies patient from study.

Randomize patients after 9 months of Maintenance to Arms VI or VII.

Late Intensification (SWOG-7825).

Arm VI: Continue OAP Maintenance, Arm V, for 3 more monthly courses.

Arm VII: POMP: VCR - 2 mg iv on day 1; PRED - 100 mg po in 2 divided doses on days 1 through 5; MTX - 10.5 mg/sqm iv on days 1 through 5 (increase dose to 15 mg/sqm then 18 mg/sqm for next two courses; start patients over 50 at 7.5 mg/sqm increasing to 10.5 and 15 mg/sqm); 6-MP - 700 mg/sqm iv on days 1 through 5 (increase dose to 1000 then 2000 mg/sqm over next two courses; start patients over 50 at 500 mg/sqm increasing to 700 then 1000 mg/sqm). Repeat each course as soon as patient recovers from previous therapy.

Rerandomize all patients in complete remission for 12 months to Arms VIII or IX.

Late Maintenance (SWOG-7826).

Arm VIII: LEV - 100 mg/sqm (to nearest 50 mg) po on 2 consecutive days q week for 6 months.

Arm IX: No further treatment.

Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules; RBD - 50 mg vials; ARA-C - 100 and 500 mg vials; VCR - 1 and 5 mg vials; MTX - 5 and 50 mg vials; 6-MP - 500 mg vials; PRED - 5 and 50 mg tablets; LEV - 50 mg tablets.

DATE SUMMARIZED: 10/78

PATIENT ACCRUAL: 00940179

6.0082 PHASE III CHEMOTHERAPY WITH HIGH VS LOW DOSE METHOTREXATE BY THE INTRATHECAL ROUTE FOR RECURRENT CNS LEUKEMIA IN CHILDREN

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7829

OBJECTIVES:

I. Compare the toxicity and efficacy of 2 doses of an intrathecal regimen of methotrexate (MTX) for children with central nervous system leukemia in relapse.

PROTOCOL ENTRY CRITERIA: Patients under 21 years old with central nervous system leukemia with demonstrable malignant cells in the spinal fluid. Patients must have received CNS prophylaxis and therapy following at least one relapse. Patients must not be known to be resistant to intrathecal MTX.

PROTOCOL OUTLINE: Randomized study.

Arm I: Induction and Maintenance. Single-agent Chemotherapy. Methotrexate, MTX, NSC-740.

Arm II: Induction and Maintenance. Single-agent Chemotherapy. MTX, high dose.

STRATIFICATION: Participating institutions; age, number of prior bone marrow relapses.

SPECIAL STUDY PARAMETERS: CSF status, EEG.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of response, relapse rate.

CURRENT STATUS: 52 patients will be entered in 2 to 3 years.

DOSAGE SCHEDULE:

Arm I: Induction. MTX - 1.5 mg/sqm intrathecal (it) twice a week until remission is obtained. Cross over patient to Arm II if progressive disease after 4 doses or no response after 6 doses. Maintenance. MTX - 1.5 mg/sqm it given at increasing time intervals of 2, 4 and 6 weeks and then q 8 weeks until relapse.

Arm II: Induction. MTX - 12 mg/sqm (maximum dose 12 mg) it twice a week for a minimum of 4 doses and a maximum of 6 doses. Enter Maintenance after 4 doses when patient is in remission, remove patient from study after 6 doses if remission is not achieved. Maintenance. MTX - 12 mg/sqm (maximum dose 12 mg) given as Arm I Maintenance.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 50 mg vials.

DATE SUMMARIZED: 11/79

6.0083 PHASE II CHEMOTHERAPY WITH AMSA FOR ACUTE LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-7970

OBJECTIVES:

I. Determine the antitumor activity of AMSA used as a continuous intravenous infusion for five days in patients with acute leukemia who have failed higher priority protocols.

II. Determine the nature and degree of toxicity of this drug by this method.

III. Determine whether heparin and hydrocortisone, HC, NSC-10483, interact to ameliorate the phlebitis associated with this agent.

PROTOCOL ENTRY CRITERIA: Patients with acute lymphoblastic or myeloblastic leukemia or the blastic phase of chronic myelocytic leukemia who have failed on higher priority protocols. Patients must have a minimum life expectancy of 4 weeks, a SWOG performance status of 3 or better. Patients must have at least 30 percent leukemic cells and a 30 percent cellular bone marrow with signs of marrow failure.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: Single-agent Chemotherapy. AMSA, NSC-249992.

Consolidation: Single-agent Chemotherapy. AMSA.

Maintenance: Single-agent Chemotherapy. AMSA.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hepatic and renal function.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: Approximately 40 patients will be entered.

DOSAGE SCHEDULE:

Induction: AMSA - 60 mg/sqm (escalating by 20 mg/sqm in subsequent sets of 4 patients until marrow hypoplasia occurs) continuous iv infusion on days 1 through 5. Enter patients with complete response to Consolidation, nonresponders are off study after 2 courses, partial responders repeat Induction until complete response or progression.

Consolidation: AMSA - 75 mg/sqm iv on days 1 through 5. Repeat once as toxicity permits. Enter patients to Maintenance.

Maintenance: AMSA - 30 mg/sqm iv on days 1 through 5. Repeat q 3 to 4 weeks as toxicity permits.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 20 and 75 mg vials.

DATE SUMMARIZED: 02/80

6.0084 HLA-MATCHED PLATELETS FOR SUPPORTIVE CARE OF PATIENTS WITH ACUTE LEUKEMIA

Schiffer, C. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7316

OBJECTIVES:

I. Evaluate the use of HLA-matched platelets for the supportive care of patients with leukemia.

II. Establish a plateletpheresis program to provide matched platelets for patients resistant to random donor platelets.

PROTOCOL ENTRY CRITERIA: All patients with leukemia.

PROTOCOL OUTLINE: Nonrandomized study.

Platelet Therapy.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Post-transfusion platelet counts, platelet survival.

END POINTS: Post-transfusion platelet count increments, amelioration of bleeding, reduction of transfusion reactions.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Platelets - Transfuse initially with platelets from random donor sources for both prophylaxis and treatment of hemorrhage. When resistance develops, transfuse with HLA-matched platelets.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 01/81

6.0085 EVALUATION OF AUTOLOGOUS PLATELETS IN SUPPORTIVE CARE OF PATIENTS WITH ACUTE LEUKEMIA

Schiffer, C. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7317

OBJECTIVES:

I. Evaluate the use of autologous platelets as supportive therapy in patients with acute leukemia in relapse.

II. Examine the feasibility of plateletpheresis of patients with leukemia in remission.

III. Preserve platelets from acute leukemia patients in remission using cryoprotective agents.

PROTOCOL ENTRY CRITERIA: Adult patients with acute leukemia in remission, particularly those who have demonstrated alloimmunization earlier in their therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Autologous Platelet Therapy. Autologous platelets stored in 5 percent DMSO at -80 degrees C.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Post-transfusion platelet counts, bleeding time.

END POINTS: Post-transfusion platelet counts, bleeding time.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Autologous Platelets - transfuse prophylactically or for active bleeding during relapse.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 01/81

6.0086 PHASE I-II CHEMOTHERAPY WITH ARA-C PLUS TDR GIVEN BY CONTINUOUS INFUSION IN PATIENTS WITH ACUTE LEUKEMIA

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PROTOCOL NUMBER(S) BCRP-7911

OBJECTIVES:

I. Determine the toxicity of combined cytosine arabinoside (ARA-C) and thymidine (TdR) administered by continuous iv infusion in patients with acute leukemia.

II. Evaluate the tolerance of continuously infused TdR at 8 g/sqm/day and ARA-C at 100, 150, and 200 mg/sqm/day.

III. Document any additive and/or synergistic effect of TdR on the antileukemic activity of ARA-C.

IV. Evaluate whether TdR increases the cytotoxicity of ARA-C in patients resistant to ARA-C.

V. Explore any correlation between histology (T, B, or null cell) and the response to treatment.

PROTOCOL ENTRY CRITERIA: Patients with acute nonlymphocytic leukemia and those with acute lymphocytic leukemia whose disease has become refractory to conventional antileukemic treatment. Patients may have received no myelosuppressive agents for at least 4 weeks prior to entry (one week for corticosteroids). Infection must be resolved or responding to treatment, and expected survival time must be at least 1 month. Renal function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878; Thymidine, TdR, NSC-21548.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, clotting tests, liver and kidney function tests, chest x-ray, bone marrow aspiration, CSF examination, terminal transferase.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

DOSAGE SCHEDULE:

TdR - 8 g/sqm/day by continuous iv infusion concurrently with and beginning 2 hours prior to ARA-C; ARA-C - 100 mg/sqm/day by continuous iv infusion, escalated to 150 and 200 mg/sqm/day in cohorts of 5 patients. Continue treatment until bone marrow hypoplasia is achieved. Withhold treatment if marrow become aplastic. Remove patient from study if disease progresses after 3 courses of treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: ARA-C - 100 and 500 mg vials; TdR - 15 g bottles.

DATE SUMMARIZED: 12/80

6.0087 PHASE I-II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE FOR PREVIOUSLY TREATED ACUTE LEUKEMIA

Van Echo, D. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America

PROTOCOL NUMBER(S) BCRP-8018

OBJECTIVES:

I. Determine the toxicity and maximally tolerated dose of aziridinylbenzoquinone (AZQ) given as a single daily dose for 7 days in patients with previously treated acute leukemia.

II. Determine the response rate and remission duration in patients treated with AZQ.

PROTOCOL ENTRY CRITERIA: Patients with bone marrow biopsy- or aspirate-confirmed diagnosis of acute undifferentiated leukemia, acute lymphocytic (ALL) or acute nonlymphocytic leukemia (ANLL) or blastic phase chronic myelocytic leukemia (B-CML). Patients must have failed conventional chemotherapy for their particular leukemia and must not be eligible for any other BCRP protocol of higher priority. Life expectancy must be at least 6 weeks and performance status at least 30-40 percent (Karnofsky scale). Patients must have recovered from prior chemotherapy or radiotherapy. Bone marrow should be normocellular, with at least 30 percent leukemic cells, and there must be evidence of progressive leukemia with signs of bone marrow failure such as anemia, granulocytopenia or thrombocytopenia. Adequate hepatic and renal function are required; bilirubin must be 1.5 mg dl or less, serum creatinine 1.5 mg dl or less.

PROTOCOL OUTLINE: Nonrandomized study. A preliminary determination of the maximal tolerated dose (MTD) of AZQ will be made.

Induction and Maintenance: Single-agent Chemotherapy. Aziridinylbenzoquinone, AZQ, NSC-182986.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Bone marrow aspirate; hematologic, liver, and kidney function tests.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, disease-free interval.

CURRENT STATUS: 14 patients will be entered.

DOSAGE SCHEDULE:

In the Phase I portion of the study, the MTD for AZQ given daily for 7 days is determined; doses are escalated from 8 mg/sqm/day to 20 mg/sqm/day in increments of 4 mg/sqm/day in cohorts of 2-3 people.

Phase II Induction: AZQ - MTD iv infusion over 30 minutes daily for 7 days. Repeat q 2-4 weeks for 3 courses; CR patients proceed to Maintenance and NR patients go off study.

Phase II Maintenance: AZQ - MTD iv infusion over 30 minutes daily for 5 days. Repeat q 4 weeks until relapse at the daily dose that induced a remission.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZQ - 10 mg vials.

DATE SUMMARIZED: 10/80

6.0088 AUTOLOGOUS STEM CELL TRANSPLANTATION & PZD CHEMOTHERAPY PLUS RADIOTHERAPY FOR ACUTE LEUKEMIA & CHRONIC GRANULOCYTIC LEUKEMIA

Dicke, K. A., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-160; MDA-DT-7524

OBJECTIVES:

I. Study the effect of chemotherapy combined with total body irradiation followed by infusion of autologous stored remission haemopoietic stem cells in acute leukemia resistant to conventional chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with adult acute leukemia, age 50 or less, in complete remission for 12 months or less having 2 or more chemotherapy courses. Patients with adult acute leukemia in complete remission for 12 months or more who have been consolidated on the Late Intensification Protocol (R142) and are receiving no chemotherapy. Patients during the benign phase of chronic granulocytic leukemia.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Radiotherapy plus Immunotherapy. Piperazinedione, PZD, NSC-135758; plus total body irradiation using the Sagitarius 25 MeV linear accelerator; plus autologous bone marrow and peripheral blood cells.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

Patients with acute leukemia will be treated after failure of any other equivalent chemotherapy for subsequent reinduction. Patients with chronic granulocyte leukemia will be treated at onset of acute blast crisis.

PZD - 25 mg/sqm iv on days minus 6 and minus 5. Total body irradiation on day 0; 850 rads are administered over 1 hour. Stem cell collection - for patients with acute leukemia in remission for 12 months or less, collect cells after completion of course of chemotherapy and following recovery of the stem cell compartment. For patients with acute leukemia in remission for 12 months or more collect cells at least 1 month after completion of Late Intensification Chemotherapy. For patients with chronic granulocytic leukemia collect stem cells (procedures are described in the protocol). Stem Cell Replacement Therapy - Stem cells - minimum dose/g equivalent to 100 million nucleated unfractionated bone marrow cells, administered 0 to 24 hours after Radiotherapy. Irradiated (2500 rads) blood components will be administered as post-transplantation supportive therapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

6.0089 PRECYTOTOXIC TREATMENT OF OLIGOLEUKEMIA WITH LITHIUM CARBONATE

Barlogie, B., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-220; MDA-DT-7719

OBJECTIVES:

I. Determine the hematologic effects of lithium carbonate in oligoleukemia.

II. Determine the efficacy of lithium carbonate in postponing the transition to and decreasing the morbidity of overt leukemia compared to MDA-DT-7312 and increasing its response to chemoimmunotherapy.

III. Identify the underlying mechanisms in in-vitro culture systems and the biochemical markers of importance in lithium therapy.

IV. Determine the toxicity of lithium carbonate in oligoleukemia.

PROTOCOL ENTRY CRITERIA: Patients with oligoleukemia or acute leukemia without previous therapy, not eligible for MDAR-155 (MDA-DT-7606). Patients with suggestive preleukemia are eligible. Patients must have normal renal function.

PROTOCOL OUTLINE: Nonrandomized study.

Precytotoxic treatment. Lithium carbonate, NSC-16895.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Polyamines in urine, activity of leukemic and normal cells in marrow, colony stimulating factor in serum and urine tested in mouse bone marrow.

END POINTS: Interval to initiation of chemotherapy, response rate, duration of response and survival to subsequent chemoimmunotherapy.

CURRENT STATUS: About 20 to 30 patients will be entered in one year.

DOSAGE SCHEDULE: Lithium carbonate - 300 mg po q 8 hours.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

6.0090 CONTINUOUS INFUSION CHEMOTHERAPY WITH ADRIAMYCIN FOR ACUTE LEUKEMIA

Bodey, G. P., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-279; MDA-DT-7818

OBJECTIVES:

I. Determine the therapeutic efficacy of continuous infusion adriamycin in patients with acute leukemia who are refractory to primary therapy.

II. Determine the toxicity of this drug administered in this fashion.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven ALL or AML leukemia not eligible for higher priority protocols who have had prior therapy with an anthracycline antibiotic but not more than 400 mg/sqm of daunomycin or 300 mg/sqm of adriamycin. Patients must have been off all chemotherapy and radiotherapy for at least 2 weeks and must have adequate cardiac and liver function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127. Continuous iv infusion in laminar air flow environment (PEPA).

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 25 patients will be entered in about 1 year.

DOSAGE SCHEDULE:

ADR - 15 mg/sqm/day by 24-hour continuous iv infusion on days 1 through 5. Repeat course q 3 weeks. Enter patient to laminar air flow room within 7 days of beginning of therapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

6.0091 PHASE II CHEMOTHERAPY WITH AMSA IN PREVIOUSLY TREATED ADULTS WITH ACUTE LEUKEMIA

Legha, S. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-284; MDA-DT-7829

OBJECTIVES:

I. Determine the efficacy of AMSA in patients with previously treated acute leukemia and in patients with chronic myelocytic leukemic blast transformation.

PROTOCOL ENTRY CRITERIA: Adult patients with acute myeloblastic or lymphoblastic leukemia who have failed on primary Induction therapy with an anthracycline or ARA-C, or patients with chronic myelocytic leukemia in blastic phase. Patients must have clearly progressive leukemia despite prior therapy (marrow blasts 30% or greater).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: SMA-12, liver function tests, EKG.

END POINTS: Response/remission rate, duration of remission.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: AMSA - 75 to 90 mg/sqm iv per day on days 1 through 5 (later changed to 1 through 7). Repeat course q 3 weeks. Increase dosage by 25% if there is no effect on marrow leukemic filtrate. Repeat course for responders as soon as leukemic regeneration is unequivocal. Remove patients with no reduction in leukemic infiltrate by day 17 of second course or patients with unacceptable toxicity from study.

Maintenance: Enter complete responders. AMSA - 40 mg/sqm/day iv on days 1 through 3. Repeat course q 3 weeks. Adjust dosage to achieve adequate myelosuppression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 00480979

6.0092 PHASE II CHEMOTHERAPY WITH DEAZAURIDINE FOR ACUTE MYELOGENOUS OR LYMPHOCYTIC LEUKEMIA

Yap, B. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-285; MDA-DT-7830

OBJECTIVES:

I. Determine the efficacy of deazauridine administered by continuous intravenous infusion to patients with acute myelogenous and acute lymphocytic leukemia.

II. Determine the qualitative and quantitative toxicity of deazauridine administered in this fashion.

III. Determine duration of response and duration of survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients 15 years old or more with histologically proven active acute leukemia not eligible for higher priority therapy. Patients must have discontinued prior therapy for 2 weeks prior to entry, and must have recovered from any associated toxicity.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Deazauridine, NSC-126849.

STRATIFICATION BY: Type of leukemia: myelogenous vs lymphocytic.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, duration of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Deazauridine - 3000 mg/sqm (reduced to 2500 mg/sqm because of excessive toxicity, June 1979) iv continuous infusion on days 1 through 5 q 3 weeks. Remove from study patients with progressive disease, unacceptable status quo, or toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/79

PATIENT ACCRUAL: 00120679

6.0093 CROPAM INDUCTION CHEMOTHERAPY AND ARA-C/TG CONSOLIDATION WITH OR WITHOUT BONE MARROW RESCUE FOR ALL, AUL, AND LYMPHOMA CELL LEUKEMIA

Dosik, G. M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-291; MDA-DT-7833

OBJECTIVES:

I. Determine the efficacy of high dose combination chemotherapy in the achievement of complete remission for patients with acute lymphoblastic leukemia, acute undifferentiated leukemia, and lymphoma cell leukemia (ALL, AUL, and LL).

II. Determine the efficacy of consolidation therapy with dosage escalation in a protected environment followed by a rotating maintenance regimen scheme in the achievement of sustained remission or cure.

III. Determine whether serial regimens (2) of megadose chemotherapy followed by autologous bone marrow rescue are more effective than the scheme outlined in the achievement of sustained remission or cure.

IV. Determine the toxicity and efficacy of a second autologous bone marrow rescue procedure after a successful recovery from a first.

V. Determine whether the use of a protected environment prophylactic antibiotic program (PEPA) will reduce the risk of infection in patients receiving megadose chemotherapy and autologous bone marrow rescue.

VI. Determine whether aggressive central nervous system prophylaxis prevents central nervous system leukemic relapse.

PROTOCOL ENTRY CRITERIA: Untreated patients over 15 years of age with bone marrow documentation of acute lymphocytic, undifferentiated, or lymphoma cell leukemia.

PROTOCOL OUTLINE: Randomized study. Patients over 60 years of age enter Arm I only. All therapy is given in a protected environment (PE).

Arm I: Induction and Consolidation.

Course I: 5-Drug Combination Chemotherapy plus Hormone Therapy. CROPAM: Cyclophosphamide, CTX, NSC-26271; Rubidazone, RBD, NSC-164011; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; L-Asparaginase, L-ASP, NSC-109229; Methotrexate, MTX, NSC-740.

Course 2: 2-Drug Combination Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878; Thioguanine, TG, NSC-752.

Course 3: 5-Drug Combination Chemotherapy plus Hormone Therapy. CROPAM, as in Course 1, with dosage escalation.

Rotating Maintenance.

Course A. 2-Drug Combination Chemotherapy. ARA-C; TG.

Course B. 2-Drug Combination and Sequentail Chemotherapy. L-ASP, MTX.

Course C. 3-Drug Combination Chemotherapy plus Hormone Therapy. CROP: CTX, RBD, VCR, PRED.

Arm II: Induction and Consolidation: Combination Chemotherapy followed by Sequential Megadose Chemotherapy with Bone Marrow Rescue in PE, followed by 3-Drug Combination Chemotherapy and CNS Prophylaxis.

Induction: CROPAM, with reduced CTX, RBD dosage.

Consolidation:

Course A. 2-Drug Combination Chemotherapy. ARA-C, TG. Upon recovery and 2 bone marrow collections, give further therapy in PEPA.

Course B. 3-Drug Mega dose Combination Chemotherapy followed by Bone Marrow Rescue. CTX; BCNU, NSC-409962; VP-16, NSC-141540.

CNS Prophylaxis: 2-Drug Sequential Chemotherapy plus Hormone Therapy followed by Single-agent Chemotherapy. MTX; Hydrocortisone, HC, NSC-10483; Citrovorum factor, CF, NSC-3590 followed by ARA-C.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 30-40 patients per year will be entered.

DOSAGE SCHEDULE:

Arm I: Induction.

Course 1. CROPAM: CTX - 1200 mg/sqm iv on day 1; RBD - 240 mg/sqm iv on day 1; VCR - 1.4 mg/sqm iv on days 1, 7, 14, and 21; PRED - 100 mg total dose po on days 1 and 14; L-ASP - 20,000 U/sqm iv on days 2, 10, and 18; MTX - 120 mg/sqm iv on days 9 and 17.

Course 2. ARA-C - 150 mg/sqm iv given over five days; TG - 50 mg/sqm po q 12 hours for 5 days.

Course 3. Following hematological recovery from ARA-C/TG, administer CROPAM: CTX - 1500 mg/sqm iv on day 1; RBD - 300 mg/sqm iv on day 1 (if bilirubin is greater than 1.5 and less than 3, reduce dose by 50%; if greater than 3, consult study coordinator); VCR - 1.4 mg/sqm iv on days 1 and 7; PRED - 100 mg po on days 1 through 7; L-ASP - 20,000 U/sqm iv; MTX - 160 mg/sqm iv on days 8 and 15. Upon hematological recovery, patients are discharged from hospital and begin Maintenance.

Rotating Maintenance:

Course A. ARA-C - 100 mg/sqm sc on days 1 through 5; TG - 50 mg/sqm po q 12 hours on days 1 through 5.

Course B. L-ASP - 20,000 U/sqm iv on day 1; MTX - 80 mg/sqm iv on day 1; MTX - 120 mg/sqm iv on day 8; L-ASP - 20,000 U/sqm iv on day 9. Continue with MTX, followed 24 hours later by L-ASP, at 7-day intervals for 4 courses of L-ASP and MTX, then give 1 cycle of Course C.

Course C. CROP: CTX - 1000 mg/sqm iv on day 1; RBD - 200 mg/sqm iv on day 1; VCR - 2.0 mg/sqm iv on days 1 and 7; PRED - 100 mg/day po for 10 days.

Repeat entire scheme of courses A, B, and C. Discontinue RBD after a total dose of 1550 mg/sqm and at that time escalate CTX to 1500 mg/sqm. Change regimens at 28-day intervals.

Arm II: Induction. CROPAM: CTX - 1000 mg/sqm iv on day 1; RBD -200 mg/sqm iv on day 1; VCR - as in Arm I; PRED - 200 mg/sqm total dose po on days 1 through 14; L-ASP - as in Arm I; MTX - as in Arm I. If complete remission is achieved enter patients to Consolidation. If leukemia persists, repeat Induction course at 20% dose escalation.

Consolidation: ARA-C - 100 mg/sqm continuous iv for 5 days; TG - as in Arm I. After recovery from ARA-C and TG, and a 25% cellular marrow with less than 5% blasts is achieved, aspirate and store bone marrow on all patients. Collect a second bone marrow, place patients in PE on prophylactic antibiotics, and treat with CTX - 1.5 g/sqm on days 1 through 4; BCNU - 300 mg/sqm iv on day 1; VP-16 - 125 mg on days 1 through 4. Administer stem cells iv on day 6. On day 60 readmit patient for a 3rd bone marrow aspiration, and a second course of CTX/BCNU/VP-16 with bone marrow rescue.

CNS Prophylaxis: Treat CNS disease via lumbar puncture and then by Ommaya reservoir. During Induction, give MTX - 15 mg intrathecal (it); HC - 20 mg it; CF - 6 mg sc 2 hours after MTX, followed by 6 mg po q 6 hours for 4 doses, q week for 4 weeks. Omit in patients receving concurrent systemic MTX. After Induction administer MTX; CF; HC once a month. Every third month, substitute ARA-C - 100 mg it.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/79

6.0094 PHASE II CONTINUOUS INFUSION CHEMOTHERAPY WITH VINDESINE FOR ACUTE LEUKEMIA AND CHRONIC MYELOGENOUS LEUKEMIA IN BLAST CRISIS

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PROTOCOL NUMBER(S) MDAR-307; MDA-DT-7854

OBJECTIVES:

I. Determine the efficacy of vindesine administered by continuous intravenous infusion to patients with acute leukemia and chronic myelogenous leukemia, blast crisis, who are refractory to primary therapy.

II. Determine the qualitative and quantitative toxicity of vindesine administered in.this fashion.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with histologically proven acute leukemia or chronic myelogenous leukemia in blast crisis. Patients must have more than 30% leukemia cells in the bone marrow, less than 100,000/cumm platelets, and/or an absolute granulocyte count of less than 1000/cumm and/or other evidence of active and progressive disease. Patients must have terminated all prior therapy at least 2 weeks prior to entry and must have recovered from any toxic effects, unless the peripheral wbc is above 5000/cumm and doubling q 2 to 3 days. Patients must have adequate liver function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Toxicity/morbidity of treatment, response/remission rate.

CURRENT STATUS: 25 patients will be entered in 6 to 12 months.

DOSAGE SCHEDULE:

DAVA - 2 mg/sqm/day as a continuous 24-hour iv infusion for 5 days. Repeat course q 3 weeks, if toxicity permits.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/79

6.0095 CHEMOTHERAPY WITH METHYL-GAG FOR PREVIOUSLY TREATED ACUTE LEUKEMIA AND OLIGO-LEUKEMIA

Keating, M. J., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-342; MDA-DT-7929

OBJECTIVES:

I. Re-evaluate methyl-GAG (MeGAG) in the treatment of previously treated patients with acute leukemia, and patients with oligoleukemia who have shown no evidence of progressive disease but require treatment because of severe bone marrow failure.

II. Study the pharmacology of methyl-GAG and its effect on polyamine synthesis and excretion.

III. Study the cytokinetic effects of methyl-GAG on leukemic cells.

PROTOCOL ENTRY CRITERIA: Patients with acute myelogenous (AML) or undifferentiated (ANL) leukemia who have relapsed or shown resistance following conventional chemotherapy, who have more than 30% bone marrow leukemia infiltrate, shown evidence of progressive disease on 2 consecutive bone marrows; and require treatment because of marrow failure or unmanageable transfusion, bleeding, hemorrhage, and patients with oligo-leukemia with less than 30% bone marrow leukemic infiltrate who have shown no evidence of progressive leukemia, who require treatment because of severe bone marrow failure. Patients with acute leukemia with a 'smoldering onset' following treatment with alkylating agents and/or radiation therapy for another malignancy can be entered after meeting above requirements.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Bone marrow studies including cytokinetics, cytogenetics, in vitro growth and P.C.C.; polyamine and MeGAG leukocyte levels.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 25 to 30 patients will be entered.

DOSAGE SCHEDULE:

MeGAG - 600 mg/sqm iv loading dose on day 1, followed by 400 mg/sqm iv on day 4 continued q 4 days until disease remission, progression or unacceptable toxicity. Give maintenance therapy to responders at the highest tolerated dose level administered q 7 days.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/79

6.0096 CHEMOTHERAPY WITH AMSA PLUS IMMUNOTHERAPY WITH AUTOLOGOUS BONE MARROW FOR RELAPSED ACUTE LEUKEMIA

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PROTOCOL NUMBER(S) MDAR-371; MDA-DT-7985

OBJECTIVES:

I. Determine complete response rate and remission rate of patients treated with this protocol and compare it with the response rate obtained with conventional AMSA treatment.

II. Determine the feasibility of dose escalation of AMSA with autologous bone marrow rescue in relapsed leukemia.

III. Determine to what degree reinfusion of autologous bone marrow can ameliorate or prevent myelosuppression and associated morbidity.

IV. Evaluate the pharmacology of high-dose AMSA by consecutive determination of serum levels.

V. Evaluate dose-limiting toxicity occurring with high-dose AMSA.

PROTOCOL ENTRY CRITERIA: Patients with acute leukemia in the first and second relapse, who have had no previous therapy with AMSA, are eligible. Patients should be less than 55 years of age and have normal liver and kidney functions.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: Single-agent Chemotherapy plus Immunotherapy. AMSA, NSC-249992; plus autologous bone marrow.

Maintenance: Single-agent Chemotherapy. AMSA.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, disease-free interval.

CURRENT STATUS: 12 patients will be entered, 3 for each dosage level.

DOSAGE SCHEDULE:

Induction: AMSA - 800, 1000, 1200 and 1400 mg/sqm iv infusion over 2-hour period/day for 4 days, 3 patients each dosage level. After remission, bone marrow is aspirated to be reinfused 3 days after completion of Chemotherapy. Consolidation upon complete remission: AMSA - 75 mg/sqm/day for 5 days; Maintenance: AMSA - 50 mg/sqm/day for 5 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

6.0097 INDIVIDUALIZED CHEMOTHERAPY OF ADULT ACUTE LEUKEMIA BASED ON PREDICTED OUTCOME TO REMISSION INDUCTION AND MAINTENANCE TREATMENT

Keating, M. J., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-381; MDA-DT-7995

OBJECTIVES:

I. Study the ability of predictive models for response to select patients likely to respond to conventional therapy with adriamycin/cytosine arabinoside/vincristine/prednisone (ADOAP).

II. Study the ability of predictive models for remission duration to select patients likely to benefit from conventional Maintenance and Intensification therapy.

III. Assess in a group of patients predicted to have a low probability of response to ADOAP whether treatment with m-AMSA/cytosine arabinoside/vincristine/prednisone will increase the response rate above that predicted.

IV. Assess whether novel Maintenance therapy with m-AMSA or allogeneic marrow transplantation will prolong remission duration in patients predicted to have short durations of remission on conventional therapy.

V. Assess whether iv BCG-MER increases the response rate or remission duration, decreases infection rate, or shortens the duration of chemotherapy-induced myelosuppression.

PROTOCOL ENTRY CRITERIA: Adult acute leukemia patients with greater than 50 percent leukemia infiltrate in the bone marrow. Patients with less than 50 percent leukemia infiltrate who are predicted to progress in less than 6 months will be entered after an observation period of 1 month. Patients with greater than 10,000 leukemic cells/cu mm, clinically significant disseminated intravascular coagulation related to the leukemic disease or organ failure resulting from leukemic infiltration will be eligible regardless of bone marrow leukemic infiltrate. Patients may not have received more than 1 course of anthracycline and/or cytosine arabinoside therapy.

PROTOCOL OUTLINE: Randomized study.

Induction: Enter all patients with a predicted probability of response of greater than 40 percent. Patients may or may not be treated in the PE. Those treated in the PE will be randomized to receive or not systemic antibiotics or systemic plus oral nonabsorbable antibiotics.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. ADOAP: Adriamycin, ADR, NSC-123127; Cytosine arabinoside, ARA-C, NSC-63878; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy plus Immunotherapy. ADR; ARA-C; VCR; PRED; BCG-MER, MER, NSC-143769.

Maintenance: CR from Arm I and Arm II are entered to Regimen A or Regimen B depending on the predicted probability of remaining in remission at 1 year.

Regimen A: Single-agent Chemotherapy plus 4-Drug Intensification Chemotherapy. m-AMSA, AMSA, NSC-249992; plus POMP: 6-Mercaptopurine, 6-MP, NSC-755; Methotrexate, MTX, NSC-740; VCR; PRED.

Regimen B: 3-Drug Combination Chemotherapy plus Hormone Therapy plus Intensification Therapy. ADOAP plus POMP plus OAP: VCR; ARA-C; PRED; plus MER.

STRATIFICATION BY: Risk for remission duration (good vs. poor) for staying in remission at 1 year.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of remission, survival rate, length of survival.

CURRENT STATUS: About 100 patients per year will be entered.

DOSAGE SCHEDULE:

Arm I: ADOAP: ADR - 55 mg/sqm iv on day 1; ARA-C - 90 mg/sqm/day for 7 days by continuous iv infusion; VCR - 2 mg iv on day 1; PRED - 100 mg/day po for 5 days. ADR and ARA-C to be increased to 75 and 110 mg/sqm, respectively, during the third course if there are no febrile episodes during the first 2 courses.

Arm II: ADOAP as in Arm I; plus MER - 0.1 mg/sqm/day for 4 days prior to institution of Chemotherapy, on days 10 and 17 of the first 3 courses of Chemotherapy, and on day 10 of subsequent courses. MER dose increased to 0.5 mg/sqm for patients with negative skin tests or with induration of less than 5 mm at 48 hours.

Regimen A: CR with poor risk for being in remission at 1 year. AMSA - 50 mg/sqm/day for 5 days each 3-4 weeks, subsequently according to tolerance. After 1 year, patients in remission will be given Intensification therapy with 3 courses of POMP (6-MP, MTX, VCR, PRED) as in Regimen B and then will discontinue treatment. Those with an HLA-identical sibling will be considered for allogenic marrow transplantation in remission.

Regimen B: CR with good risk for being in remission at 1 year. Three consolidation courses of ADOAP. The dosage of ADR and ARA-C for patients outside the PE will be, respectively, 30 mg/sqm on day 1 and 70 mg/sqm/day for 5 days sc. Patients will then receive OAP, with the ARA-C dose based on the response of the patient to the Consolidation courses of ADOAP. The next 3 courses of therapy will be with POMP: 6-MP - 700 mg/sqm/day for 5 days; MTX - 10.5 mg/sqm/day for 5 days; VCR - 2 mg iv on day 1; and PRED - 200 mg/day for 5 days po. This will be followed by 3 cycles of ADOAP, 3 cycles of OAP, and 3 cycles of POMP, after which only MER therapy will be administered, monthly as long as tolerated.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/80

6.0098 SURGERY AND/OR CHEMOTHERAPY WITH DRB AND/OR IMMUNOTHERAPY WITH MER AND MONONUCLEAR CELL TRANSFUSIONS FOR HAIRY CELL LEUKEMIA

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PROTOCOL NUMBER(S) MDAR-399; MDA-DT-8010

OBJECTIVES:

I. Stage patients with hairy cell leukemia based on the degree of derangement of the immune system and bone marrow function.

II. Attempt the restoration of such dysfunctions using the individually determined administration of methanol extraction residue (MER) BCG, mononuclear cell transfusions (MNCT), and splenectomy or chemotherapy with daunorubicin (DRB).

PROTOCOL ENTRY CRITERIA: Patients with established diagnosis of hairy cell leukemia. Patients must have at least 80 percent of normal pulmonary function. Patients must not have a history of serious pulmonary impairment or congestive heart failure or ischemic heart disease. Patients must receive no treatment for six weeks prior to entry. Patients who have received prior mycobacterial agents and those with a positive PPD skin test are eligible but will receive a reduced MER dose.

PROTOCOL OUTLINE: Nonrandomized study. Patients are placed in Stage I, II, and III or IV based on the following criteria: hemoglobin, platelets, absolute neutrophiles, history of recurrent or unusual infections, and immune dysfunction. Stage I and II patients enter Regimen A; Stage III enter Regimen B, and Stage IV enter Regimen D or E.

Regimen A: Serial evaluation q 6 months or 3 months. No treatment.

Regimen B: Immunotherapy. MER-BCG, MER, NSC-143769. Enter failures to Regimen C.

Regimen C: Immunotherapy. Mononuclear cell transfusions plus MER. Enter patients who fail to achieve CR to Regimen D; failures ineligible for Regimen D Surgery may enter Regimen E.

Regimen D: Surgery. Splenectomy.

Regimen E: Single-agent Chemotherapy. Daunorubicin, DRB, NSC-82151.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests, PPD skin test, immune system evaluation, bone marrow function evaluation.

END POINTS: Response/remission rate, duration of response.

CURRENT STATUS: Approximately 20 patients will be entered per year.

DOSAGE SCHEDULE:

Regimen A: Serial evaluation only, every 6 months (Stage I) or 3 months (Stage II).

Regimen B: MER - 0.5 mg/sqm (0.1 mg/sqm for patients with positive PPD or previous BCG treatment) iv q week with increments of 33 percent of previous dose for 6 weeks. Patients showing CR or significant improvement receive Maintenance treatment with MER given weekly for 3 courses, then q 2 weeks for 6 courses. Failures go to Regimen C.

Regimen C: Mononuclear cell transfusions (MNCT) begin 2 weeks after the last Regimen B MER dose. MNCT - a serial of 3 daily; plus MER on day 2 at last dose employed in Regimen B, at least 1 hour apart from MNCT. Repeat series in 2 weeks. Patients achieving CR receive Maintenance MER as in Regimen B. Failures go to Regimen D; those ineligible for Surgery may go to Regimen E.

Regimen D: Splenectomy.

Regimen E: DRB - 40 mg/sqm/day iv continuous infusion for 4 days. Patients who fail to achieve CR receive a second course of Chemotherapy 21 days after the first course, with the dose increased by 20 percent if there is no evidence of toxicity. Failures after 2 courses are candidates for alternate treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

6.0099 PHASE I-II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR ACUTE LEUKEMIA

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PROTOCOL NUMBER(S) MDAR-411; MDA-DT-8030

OBJECTIVES:

I. Determine the efficacy of anthracenedione (dihydroxyanthracenedione) by intermittent infusion in patients with acute leukemia.

II. Determine the optimal dose of anthracenedione in this disease.

III. Determine the qualitative and quantitative toxicity of the drug administered in this fashion.

IV. Determine duration of response and duration of survival in patients receiving this treatment.

PROTOCOL ENTRY CRITERIA: Adult patients with acute myeloblastic, acute lymphoblastic, or acute undifferentiated leukemia or chronic myelocytic leukemia in blastic phase who have failed regimens of higher priority. Patients should have clear evidence of progressive leukemia; the absolute bone marrow infiltrate should be greater than 50 percent (unless the absolute peripheral blast count is greater than 10,000 per microliter), or there should be evidence of organ disfunction due to leukemic infiltration or coagulation abnormalities. Patients should have received no chemotherapy during the two weeks preceding entry.

PROTOCOL OUTLINE: Nonrandomized study. Chemotherapy is concurrent with infection prophylaxis as per MDA-DT-80-01.

Single-agent Chemotherapy. Anthracenedione, Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Bone marrow aspiration and biopsy.

END POINTS: Response/remission rate, duration of response, duration of survival, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 25 evaluable patients will be entered.

DOSAGE SCHEDULE:

DHAD - 4 mg/sqm daily for 5 days for the first 3 patients. If inadequate anti-leukemic effect without excess non-hematopoietic toxicity is seen, the starting dose will be increased to 5 mg/sqm daily for 5 days for the next 3 patients. A bone marrow aspiration and biopsy is performed on day 18. If the marrow shows cellularity above 30 percent and blast above 30 percent, a second course is started on day 21. If the marrow shows no anti-leukemic effect, a second course is started at a dose increase of 1 mg/sqm/day on day 21. If the criteria for retreatment are not met, bone marrow examinations are performed twice weekly. A second course of Chemotherapy is started at evidence of recovery. Patients who show rapidly progressive disease before day 21 have a bone marrow aspiration before day 21; a second course of therapy is begun immediately at a dose increase of 1 mg/sqm/day. All patients receive 3 courses of treatment, except those with rapidly progressive disease after 2 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

6.0100 BONE MARROW RESTORATION WITH LITHIUM CARBONATE AND MER-BCG FOR OLIGOLEUKEMIA AND PRE-LEUKEMIA

Quesada, J., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-414; MDA-DT-8035P

OBJECTIVES:

I. Define the hematological and immunological effects of a sequential treatment with lithium carbonate and the methanol extraction residue (MER) of bacillus Calmette-Guerin (BCG) in patients with oligoleukemia.

II. Determine the effect of this treatment on survival and incidence of infectious complications in these patients.

PROTOCOL ENTRY CRITERIA: Patients with a hematological picture compatible with oligoleukemia as defined by an absolute leukemic bone marrow infiltrate of under 50 percent and peripheral blast count of less than 5000 blasts per cumm; or patients with acute leukemia in smoldering relapse after a well-defined complete remission who are not candidates for higher priority treatment; or patients with hematological abnormalities suggestive of a preleukemic disorder such as bone marrow dysplasia, agranulocytosis with monocytosis, or pancytopenia. Patients must have at least 80 percent of normal pulmonary function and adequate cardiac reserve.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy plus Bone Marrow Restoration. MER-BCG, BCG, NSC-143769; Lithium carbonate, NSC-16895.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response rate, survival, incidence of infectious complications.

CURRENT STATUS: 20 patients will be entered.

DOSAGE SCHEDULE:

BCG - 0.5 mg/sqm iv weekly for 4 courses followed (if no improvement occurs) by Lithium carbonate - 900 mg po in 3 divided doses daily for 4 weeks. Thereafter, alternate BCG and Lithium carbonate, giving BCG q other week and Lithium carbonate daily for 7 days q other week. Patients with a history of prior BCG or with positive PPD should receive BCG at a dose of 0.1 mg/sqm. After 16 weeks, unresponsive patients enter protocol MDA-DT-79-08; responding patients continue on this protocol for a maximum of 12 BCG doses. 10 patients are treated on the above schedule; 10 patients are treated on the above dosage and time schedule with the order of drug administration reversed (i.e., Lithium carbonate followed by BCG).

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

6.0101 HIGH-DOSE COMBINATION CHEMOTHERAPY WITH CTX/BCNU/VP-16 PLUS AUTOLOGOUS BONE MARROW TRANSPLANTATION FOR LEUKEMIA IN RELAPSE

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PROTOCOL NUMBER(S) MDAR-415; MDA-DT-8041

OBJECTIVES:

I. Determine the efficacy of megadose chemotherapy with cyclophosphamide, BCNU, and VP-16 with autologous bone marrow rescue in relapse acute leukemia resistant to conventional chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with acute myelogenous leukemia (M1-M5) and acute lymphocytic leukemia in the first or second relapse who have bone marrow, aspirated at a time of solid remission (at least 2-3 months from an overt leukemic phase), in storage.

PROTOCOL OUTLINE: Nonrandomized study. Regimen A therapy is given in a protected environment. Patients who achieve CR are discharged from the protected environment and enter Maintenance.

Regimen A: Induction: 3-Drug Combination Chemotherapy plus Bone Marrow Rescue. Cyclophosphamide, CTX, NSC-26271; BCNU, NSC-409962; VP-16213, VP-16, NSC-141540; plus autologous bone marrow cells.

Regimen B: Maintenance: 2-Drug Combination Chemotherapy. CTX; VP-16.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests, bone marrow function tests.

END POINTS: Response/remission rate.

CURRENT STATUS: About 20 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Therapy is administered in a protected environment. CTX - 1.5 g/sqm iv on days 1, 2, and 3; BCNU - 300 mg/sqm iv on day 1; VP-16 - 200 mg/sqm iv in 2 divided doses 12 hours apart on days 1, 2, and 3; bone marrow rescue - at least 0.5 x 10 to the eighth cells/kg on day 7. Patients who show a partial response receive another course, providing there is enough bone marrow available. Patients who show a partial response without adequate marrow in storage and patients in complete remission are discharged from the protected environment and enter Regimen B Maintenance. Nonresponding patients go off study.

Regimen B: Maintenance: CTX - 500 mg/sqm iv on day 1; VP-16 - 75 mg/sqm iv daily for 5 days.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

6.0102 CHEMOTHERAPY WITH PZD/MTX PLUS RADIOTHERAPY PLUS BONE MARROW TRANSPLANTATION FOR ADULT ACUTE LEUKEMIA IN REMISSION

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PROTOCOL NUMBER(S) MDAR-416; MDA-DT-7970

OBJECTIVES:

I. Evaluate the effect of allogeneic bone marrow transplantation on disease-free survival of patients with acute leukemia in remission, when it is given after chemotherapy with piperazinedione (PZD) and total body irradiation.

PROTOCOL ENTRY CRITERIA: Patients at M.D. Anderson in complete remission following treatment on protocol MDA-DT 79-95, who have poor risk factors for remission duration, and patients with AML, AUL and ALL in second remission if alternative therapies are less promising. Referred patients, in first and second remission after treatment with Induction regimens other than MDA-DT 79-95, will be considered.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Radiotherapy plus Bone Marrow Transplantation. Piperazinedione, PZD, NSC-135758; plus total body irradiation; plus allogeneic bone marrow infusion given in a protected environment, followed by Methotrexate, MTX, NSC-740.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Length of disease-free survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

PZD - 25 mg/sqm on two consecutive days; following a 4-day rest period, total body irradiation is administered, 6 doses of 170 rads twice daily for 3 days. After the last irradiation dose, bone marrow is infused. MTX - 10 mg/sqm is given on day 1 following bone marrow infusion and on days 3, 6, 11, 18, and 25, and weekly thereafter for a total of 100 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

6.0103 BONE MARROW TRANSPLANTATION VS CHEMOTHERAPY WITH CTX PLUS RADIOTHERAPY FOR LEUKEMIA

Gale, R. P., (213-825-0825) University of California, Los Angeles, School of Medicine, Division of Hematology and Oncology, Los Angeles, California, 90024, United States of America

PROTOCOL NUMBER(S) UCLA-BMT-40

OBJECTIVES:

I. Evaluate the role of allogeneic (HLA-identical) bone marrow transplantation vs. conventional therapy in patients with acute myelogenous leukemia (AML) in first remission, in adults with acute lymphoblastic leukemia (ALL) in first remission, in children with ALL in second or later remission, and in patients with chronic myelogenous leukemia (CML) in the chronic phase.

PROTOCOL ENTRY CRITERIA: Patients with ALL in first remission, adults with ALL in first remission, children with ALL in second (or later) remission, patients with CML in the chronic phase.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Radiotherapy plus Bone Marrow Transplantation. Cyclophosphamide, CTX, NSC-26271; total body radiation; allogeneic (HLA-identical) marrow transplantation.

STRATIFICATION BY: None

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Remission, survival.

CURRENT STATUS: 170 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

CTX - 60 mg/kg/day for 2 days; total body radiation - 1000 rads; allogeneic (HLA-identical) marrow transplantation.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

6.0104 IMMUNOTHERAPY WITH IMMUNE GAMMA GLOBULIN (LEUKOGLOBULIN) ALONE AND WITH SINGLE-AGENT CHEMOTHERAPY (DNM, MTX, CLB OR VCR) FOR LEUKEMIA

Lozzio, B. B., (615-971-3226) University of Tennessee College of Medicine, Memorial Research Center, Dept. of Medical Biology, 1924 Alcoa Highway, Knoxville, Tennessee, 37920, United States of America

PROTOCOL NUMBER(S) UTENN-LEU-1

OBJECTIVES:

I. Determine the qualitative and quantitative toxicity of xenogeneic (goat) immune gamma-globulin (antibody to the human leukemia stem cell line K-562) in patients with terminal leukemia.

II. Determine the therapeutic efficacy of leukoglobulin in patients with AML, CML, AMML and ALL.

III. Evaluate the synergism of leukoglobulin with daunomycin (DNM), methotrexate (MTX), chlorambucil (Leukeran; CLB), and vincristine (Oncovin; VCR).

This is a cooperative study with S. Krauss, M.D., C.B. Lozzio, M.D. (same institution) and Josefa Izquierdo, M.D. and co-workers, Juncal 2579, Buenos Aires, Argentina. Phone: 84-5289.

PROTOCOL ENTRY CRITERIA: Patients in the terminal stage of AML, AMML, CML, ALL and other rare types of leukemias, and patients with leukemia refractory to available therapy. First priority: AML and CML in blastic crisis. Excluded are patients with severe allergic diseases, liver and/or renal insufficiency, and heart failure.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. Leukoglobulin: immune goat gammaglobulins.

Arm II: Immunotherapy plus Single-agent Chemotherapy. Synergism. Leukoglobulin plus low doses of either: Daunomycin, DNM, NSC-82151; or Methotrexate, MTX, NSC-740; or Chlorambucil, CLB, NSC-3088; or Vincristine, VCR, NSC-67574.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Liver and renal function tests; skin and hemagglutination tests with the goat antibody; daily peripheral blood cell values; bone marrow cell differential as deemed appropriate; patient serum antibody level (if any) to goat gammaglobulins monthly; diuresis; BUN, serum uric acid, bilirubin and enzyme (LD, GOT, GPT and GGTP) levels weekly.

END POINTS: Toxicity and/or morbidity of treatment such as allergic reactions, significant levels of serum antibody to goat proteins; response/remission rate; duration of the remission as determined by the peripheral blood cell and bone marrow counts and modification of the hepato-splenomegaly and adenopathies, if present.

CURRENT STATUS: Six patients have entered Arm I and II as of May 1980. At least 30 patients will be treated and the results evaluated in Arm I and II.

DOSAGE SCHEDULE:

Arm I: Leukoglobulin - 2, 4, 8, 10 and 15 mg/kg iv weekly for 5 weeks. Two or three patients at each dose level until toxicity (if any) is observed.

Arm II: Leukoglobulin plus DNM - 15 mg/sqm once a week iv; or MTX - 10 mg/sqm once a week iv; or CLB - 0.1 mg/kg daily for 5 days po; or VCR - 1.0 mg/sqm once a week iv. Administration of each chemotherapeutic agent may begin with the second or third dose of the antibody.

All patients will be given 2.5-3 liters of fluids orally or parenterally, allopurinol (500-900 mg daily) for 5 weeks beginning 7 days after the first injection of the antibody, hydrocort (20-200 mg iv), benadryl (50-80 mg daily), epinephrin for possible anaphylactic shock, and prednisone (0.5 mg/kg daily) for other allergic reactions.

Maintenance: No further treatment against leukemia; standard supporting therapy and other treatments as deemed appropriate.

Dosage modifications for toxicity are given.

DOSAGE FORMS: The goat antibody is available lyophilized and as precipitated gamma-globulin fraction (greater than 65 percent IgG) in 33 percent saturated ammonium sulfate at a concentration of 50 mg/ml.

Summary as provided by investigator.

DATE SUMMARIZED: 05/80

PATIENT ACCRUAL: 00040579

6.0105 INDUCTION CHEMOTHERAPY AND ANTIBIOTIC THERAPY WITH AND WITHOUT LITHIUM CARBONATE FOR ACUTE LEUKEMIA

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PROTOCOL NUMBER(S) CAN-NCIC-IC1

OBJECTIVES:

I. Determine whether lithium carbonate will shorten the duration of granulocytopenia following remission Induction chemotherapy for acute leukemia.

II. Determine whether the addition of lithium carbonate to prophylactic trimethoprim/sulfamethoxazole will reduce the incidence of fever and infection and increase remission induction rate following remission Induction chemotherapy for acute leukemia.

PROTOCOL ENTRY CRITERIA: Patients, aged 15 and over, with acute leukemia requiring aggressive Induction chemotherapy that is expected to produce granulocytopenia (less than 1000/cumm) for 2-3 weeks. Patients with acute lymphoblastic leukemia who are being treated with vincristine and prednisone are not eligible. Patients with acute myeloblastic leukemia who require reinduction for relapse are eligible. Patients must not be allergic to trimethoprim. They must have no significant concomitant disease (particularly renal disease) and no history of another primary cancer (except basal or squamous cell carcinoma of the skin).

PROTOCOL OUTLINE: Randomized study. Patients who relapse may be rerandomized for reinduction.

Arm I: Induction Chemotherapy plus Antibiotic Therapy plus Attenuation of Chemotherapy-induced Granulocytopenia. Induction Chemotherapy as prescribed by the participating institution; plus Trimethoprim, NSC-106568; Sulphamethoxazole; plus Lithium carbonate, NSC-16895.

Arm II: Induction Chemotherapy plus Antibiotic Therapy. Induction Chemotherapy as prescribed by the participating institution; plus Trimethoprim; Sulphamethoxazole.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; chest x-ray; microbiology studies: blood, sputum, and urine cultures; lithium levels.

END POINTS: Remission induction rate, duration of granulocytopenia, number of febrile days of temperature greater than 38 degrees centigrade, frequency of documented clinical infection.

CURRENT STATUS: 126 patients will be entered over a 2-year period.

DOSAGE SCHEDULE:

Arm I: Lithium carbonate - 900 mg/day po in 3 divided doses. Begin Lithium carbonate the final day of Chemotherapy and continue until granulocyte count is over 1000/cumm. Trimethoprim and Sulphamethoxazole is started on day 1 and continued until remission is achieved. (Septra and Bactrim are commercially available preparations of the combination Trimethoprim/Sulphamethoxazole. Patients should receive 2 pills twice a day. Patients allergic to Sulphamethoxazole receive Trimethoprim alone, 200 mg twice a day.)

Arm II: Induction Chemotherapy plus Trimethoprim and Sulphamethoxazole as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Lithium carbonate - 300 mg tablets; Trimethoprim - 100 mg tablets.

DATE SUMMARIZED: 01/81

6.0106 INDUCTION CHEMOTHERAPY WITH DCMP (DRB/ARA-C/6-MP/PRDL) OR VP (VCR/PRDL) PLUS MAINTENANCE WITH ARA-C/6-MP WITH OR WITHOUT LEV FOR ACUTE LEUKEMIA

Maekawa, T., Gunma University School of Medicine, The Third Dept. of Internal Med., 3-39-15 Showa-Cho, Maebashi, Gunma 371, Japan

PROTOCOL NUMBER(S) JAP-KLSG-1

OBJECTIVES:

I. Compare the duration of complete remission for patients with acute leukemia who are on Maintenance with cytosine arabinoside/6-mercaptopurine with or without levamisole immunotherapy following Induction with DCMP (daunorubicin, cytosine arabinoside, 6-mercaptopurine and prednisolone) for ANLL and VP (vincristine, prednisolone) for ALL.

PROTOCOL ENTRY CRITERIA: Patients with acute lymphocytic and acute nonlymphocytic leukemia who have received no previous chemotherapy, radiotherapy or immunotherapy.

PROTOCOL OUTLINE: Study randomized for Maintenance only.

Induction: Patients with acute nonlymphocytic leukemia receive Regimen A; patients with acute lymphocytic leukemia receive Regimen B.

Regimen A: 3-Drug Combination Chemotherapy plus Hormone Therapy. DCMP: Daunorubicin, DRB, NSC-82151; Cytosine arabinoside, ARA-C, NSC-63878; 6-Mercaptopurine, 6-MP, NSC-755; plus Prednisolone, PRDL, NSC-9900.

Regimen B: Single-agent Chemotherapy plus Hormone Therapy. VP: Vincristine, VCR, NSC-67574; plus PRDL.

Maintenance:

Arm I: 2-Drug Combination Chemotherapy. ARA-C; 6-MP.

Arm II: 2-Drug Combination Chemotherapy plus Immunotherapy. ARA-C; 6-MP; plus Levamisole, LEV, NSC-177023.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, disease-free interval, recurrence rate, survival rate, length of survival.

CURRENT STATUS: 24 patients have been entered as of December 1979.

DOSAGE SCHEDULE:

Induction:

Regimen A: DCMP: DRB; ARA-C; 6-MP; PRDL. Dosage schedule not provided.

Regimen B: VP: VCR; PRDL. Dosage schedule not provided.

Maintenance:

Arm I: ARA-C - 1.5 mg/kg; 6-MP - 2 mg/kg by the modified method of Peterson and Bloomfield (Lancet, 23:158, 1977).

Arm II: ARA-C and 6-MP as in Arm I; plus LEV - 150 mg/kg daily for 3 consecutive days q 2 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by the investigator.

DATE SUMMARIZED: 08/80

6.0107 C. PARVUM IMMUNOTHERAPY FOR MAINTENANCE OF PATIENTS WITH ACUTE NONLYMPHOBLASTIC LEUKEMIA IN COMPLETE REMISSION

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PROTOCOL NUMBER(S) SAFR-CT-LEU-1

OBJECTIVES:

I. Compare, in terms of survival, Maintenance chemotherapy alone vs. Maintenance chemotherapy plus C. parvum immunotherapy in adult patients with acute leukemia.

II. Compare in these patients in vitro bone marrow culture, hematopoietic reserve and mitogenic response together with in vivo skin testing as indices of hematologic and immunologic reconstitution.

PROTOCOL ENTRY CRITERIA: Adults with acute lymphoblastic or acute nonlymphoblastic leukemia in complete remission following chemotherapy on other protocols (SAFR-ANLL-1 and SAFR-CT-LEU-3).

PROTOCOL OUTLINE: Randomized study. Patients achieving a second complete remission following first remission transplantation, early Intensification, or late Intensification on other University of Cape Town protocols are randomized to Arm I or Arm II.

Arm I: Single-agent Immunotherapy. Corynebacterium parvum, Burroughs-Wellcome (Coparvax), C. parvum, NSC-220537.

Arm II: Controls.

STRATIFICATION BY: Disease: AML vs. ALL; prior therapy: transplantation vs. chemotherapy, transplantation vs. early and late Intensification.

SPECIAL STUDY PARAMETERS: In vitro marrow culture, nucleolar antigen, immunologic monitoring with lymphocyte mitogenic response, in vivo skin tests.

END POINTS: Disease-free interval, quarterly response to mitogens, survival.

CURRENT STATUS: 44 patients were entered as of October 1980.

DOSAGE SCHEDULE:

Arm I: C. parvum - 2.5 mg iv weekly for 3 weeks. Maintenance Chemotherapy in week 4.

Arm II: Injections of diluent, as in Arm I, but without C. parvum. Maintenance as in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: C. parvum - formalin-fixed suspension.

DATE SUMMARIZED: 01/81

SECTION 7

LUNG TUMORS

7A. SMALL CELL (OAT CELL) LUNG TUMORS

CLB-7781	PHASE III MTX, ADR, CCNU, CTX, VCR CHEMOTHERAPY IN TWO COMBINATIONS PLUS RADIOTHERAPY AND MER IMMUNOTHERAPY FOR OAT CELL CARCINOMA OF THE LUNG	7.0001
CLB-7782	PHASE III COMBINATION CHEMOTHERAPY WITH MACC VS MACC PLUS RADIOTHERAPY VS CCV-AV FOR EXTENSIVE SMALL CELL CARCINOMA OF THE LUNG	7.0002
CLB-8073	PHASE II CHEMOTHERAPY WITH MGBG FOR REFRACTORY SMALL CELL CARCINOMA OF THE LUNG	7.0003
EST-PC-579	PHASE II HIGH-DOSE INDUCTION CHEMOTHERAPY WITH CTX/MTX/VP-16 FOR DISSEMINATED SMALL CELL CARCINOMA OF THE LUNG	7.0004
EST-1578	PHASE III STANDARD-DOSE CCM (CTX/CCNU/MTX) VS HIGH-DOSE CCM WITH OR WITHOUT AVP MAINTENANCE FOR SMALL CELL LUNG CANCER	7.0005
EST-2579	PHASE III CHEMOTHERAPY WITH PALA, AMSA, VM-26, AND NCS AS SINGLE AGENTS IN SMALL CELL LUNG CANCER	7.0006
NCOG-2O61	PHASE III CHEMOTHERAPY WITH VP-16/ADR/MTX, CTX/CCNU/VCR/PCB PLUS RADIOTHERAPY FOR UNDIFFERENTIATED SMALL CELL ANAPLASTIC LUNG CANCER	7.0007
NCOG-2O91	PHASE III 7-DRUG VS 9-DRUG CHEMOTHERAPY IN EXTENSIVE DISEASE & LATE CONSOLIDATION RADIOTHERAPY IN LIMITED DISEASE SMALL CELL CARCINOMA	7.0008
SEG-LUN-P32	PHASE II PILOT CHEMOTHERAPY WITH VP-16/MTX/CF/CCNU FOR RECURRENT OR PROGRESSIVE OAT-CELL LUNG CARCINOMA	7.0009
SEG-78LUN252	PHASE II INDUCTION WITH HIGH-DOSE CAV (CTX/ADR/VCR) VS CAV PLUS VP-16 AND CAV CONSOLIDATION FOR METASTATIC SMALL CELL LUNG CANCER	7.0010
SEG-78LUN328	PHASE III CTX/ADR/VCR THERAPY ALONE OR WITH RADIOTHERAPY FOLLOWED BY VP-16/HMM OR MTX/CF/VP-16/HMM FOR SMALL CELL LUNG CANCER	7.0011
SEG-79LUN252	PHASE II COMPARISON OF HIGH-DOSE CAV (CTX/ADR/VCR) VS CONVENTIONAL-DOSE CAV PLUS VP-16213 IN GOOD-RISK METASTATIC SMALL CELL LUNG CARCINOMA	7.0012
SWOG-7828	PHASE III VCR/MTX/VP-16 VS VCR/ADR/CTX OR BOTH PLUS CRANIAL RADIOTHERAPY FOR EXTENSIVE SMALL CELL CARCINOMA OF THE LUNG	7.0013
SWOG-7924	PHASE III CHEMOTHERAPY WITH ADR/CTX/MTX/VCR/VP-16 PLUS RADIOTHERAPY FOR SMALL CELL CARCINOMA OF THE LUNG	7.0014
SWOG-8009	PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE FOR REFRACTORY SMALL CELL LUNG CANCER	7.0015

BCRP-7705	INTENSIVE COMBINATION CHEMOTHERAPY WITH OR WITHOUT PROPHYLACTIC WHOLE BRAIN IRRADIATION FOR SMALL CELL CARCINOMA OF THE LUNG	7.0016
BCRP-8020	INTENSIVE COMBINATION CHEMOTHERAPY WITH ACE (ADR/CTX/VP-16) VS ACE-II (ADR/CTX/HD INFUSION VP-16) FOR SMALL CELL CARCINOMA OF THE LUNG	7.0017
BCRP-8024	PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE (AZQ) FOR PREVIOUSLY TREATED SMALL CELL CARCINOMA	7.0018
MAYO-782003	CONTINUOUS VS ALTERNATING VOCAP (VCR/VP-16/CTX/ADR/CACP) VS VCP (CTX/CACP/VP-16) FOR EXTENSIVE SMALL CELL LUNG CANCER	7.0019
MAYO-792001	CHEMOTHERAPY WITH CTX, CCNU, VP-16, VCR, CACP, MTX, ADR AND VBL, AND/OR RADIOTHERAPY FOR HIGH AND LOW TUMOR BURDEN SMALL CELL LUNG CANCER	7.0020
MAYO-792004	CHEMOTHERAPY WITH C2AV2 (CTX/CCNU/ADR/VP-16/VCR) FOLLOWED BY RADIOTHERAPY PLUS CHEMOTHERAPY FOR LIMITED SMALL CELL LUNG CANCER	7.0021
MAYO-792051	CHEMOTHERAPY WITH CCM PLUS ALTERNATING CCM/ADR/VCR VS CCM/ADR/VCR/VP-16 FOR EXTENSIVE SMALL CELL LUNG CANCER	7.0022
MDAR-329	MEGADOSE ECHO, BONE MARROW TRANSPLANTATION, BRAIN IRRADIATION, AND NUTRITIONAL THERAPY IN PEPA FOR SMALL CELL BRONCHOGENIC CARCINOMA	7.0023
MDAR-329R	HIGH-DOSE COMBINATION CHEMOTHERAPY WITH VP-16/CTX/VCR PLUS AUTOLOGOUS BONE MARROW TRANSPLANT FOR LIMITED OAT CELL CARCINOMA	7.0024
MDAR-368	COMBINATION CHEMOTHERAPY WITH NM/PCB/MTX/CF FOR PREVIOUSLY TREATED PATIENTS WITH EXTENSIVE SMALL CELL ANAPLASTIC LUNG CANCER	7.0025
MDAR-369	CHEMOTHERAPY BY CONTINUOUS INFUSION OF VP-16213 OR VM-26 FOR ADVANCED OAT-CELL LUNG CANCER IN ADULTS	7.0026
MDAR-383	PROPHYLACTIC ANTIBIOTICS IN PE DURING CONSOLIDATION WITH CTX/VP-16/MTX/CF AFTER INDUCTION WITH VCR/IPP/ADR FOR SMALL CELL BRONCHOGENIC CARCINOMA	7.0027
MDAR-384	PHASE II EVALUATION OF VINDESINE PLUS CIS-PLATINUM FOR REFRACTORY SMALL CELL CARCINOMA OF THE LUNG	7.0028
MSKCC-7891R	COMBINATION CHEMOTHERAPY WITH ADR, CTX, VCR, CACP, VP-16, CCNU, PCB PLUS RADIOTHERAPY WITH/WITHOUT THYMOSIN FOR SMALL CELL CARCINOMA OF THE LUNG	7.0029
MSKCC-8024	PILOT COMBINATION CHEMOTHERAPY WITH ADR/BCNU/VP-16 PLUS IMMUNOTHERAPY FOR SMALL CELL LUNG CARCINOMA IN FIRST RELAPSE	7.0030
NCI-77-C-171	PHASE I-II HEMIBODY RADIOTHERAPY FOR PROGRESSIVE SMALL CELL CARCINOMA OF THE LUNG	7.0031
NCI-80-C-67	PILOT COMBINATION CHEMOTHERAPY, RADIOTHERAPY AND IMMUNOTHERAPY FOR EXTENSIVE SMALL CELL LUNG CARCINOMA	7.0032
WPL-7621	CHEMOTHERAPY WITH VAV (VP-16/ADR/VCR) AND CCM (CTX/CCNU/MTX), RADIOTHERAPY, AND LEV IMMUNOTHERAPY FOR OAT-CELL LUNG CARCINOMA	7.0033
NCCTG-792052	VOCA (VP-16/VCR/CTX/ADR) VS OCA (VCR/CTX/ADR) PLUS RADIOTHERAPY FOR LIMITED STAGE SMALL CELL LUNG CANCER	7.0034
NUTR-7901	PHASE III CHEMOTHERAPY WITH CTX/ADR/VCR PLUS VP-16/MTX/CF WITH/WITHOUT TOTAL PARENTERAL NUTRITION FOR SMALL CELL ANAPLASTIC LUNG CARCINOMA	7.0035
EORTC-08764	ADR/MTX/CTX/CCNU CHEMOTHERAPY PLUS C. PARVUM IMMUNOTHERAPY WITH AND WITHOUT DEHYDROEMETINE/VCR/BLEO FOR SMALL CELL LUNG CANCER	7.0036

ITA-MIL-LC793 COMBINATION CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE/METHOTREXATE/CCNU WITH VS WITHOUT VP-16213 FOR OAT CELL LUNG CANCER 7.0037

7B. LUNG TUMORS—GENERAL

CLB-8071 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED NON-SMALL CELL CARCINOMA OF THE LUNG 7.0038
EST-2575-IIIR2 PHASE III CTX/BLEO/CACP VS ADR/5-FU/CACP VS MITO/VBL/CACP VS CTX/ADR/CACP FOR METASTATIC NON-SMALL CELL LUNG CANCER 7.0039
EST-3578 LOCALIZED RADIOTHERAPY WITH VS WITHOUT CAMP (CTX/ADR/MTX/PCB) CHEMOTHERAPY OR HALF-BODY RADIOTHERAPY FOR THORACIC NON-SMALL CELL LUNG CANCER 7.0040
NCOG-2N83 PHASE II CHEMOTHERAPY WITH AMSA FOR METASTATIC OR RECURRENT LUNG CANCER 7.0041
RTOG-7807 RADIOTHERAPY WITH NEUTRONS FOR LOCALIZED NONRESECTABLE NON-OAT CELL LUNG CARCINOMA 7.0042
RTOG-7811 PHASE III ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE WITH CONCURRENT RADIOTHERAPY FOR UNRESECTABLE LUNG CARCINOMA 7.0043
RTOG-7907 PHASE III PHOTON VS NEUTRON VS PHOTON/NEUTRON RADIOTHERAPY FOR LOCALIZED, INOPERABLE NON-OAT CELL LUNG CANCER 7.0044
RTOG-7917 PHASE III RADIOTHERAPY VS RADIOTHERAPY PLUS MISONIDAZOLE FOR LOCALLY ADVANCED NON-OAT CELL LUNG CANCER 7.0045
RTOG-7925 PHASE III RADIOTHERAPY WITH AND WITHOUT MISONIDAZOLE FOR LOCALLY ADVANCED NON-OAT CELL LUNG CANCER 7.0046
RTOG-7927 PHASE III POSTOPERATIVE RADIOTHERAPY WITH/WITHOUT LEVAMISOLE IMMUNOTHERAPY FOR NON-OAT CELL LUNG CARCINOMA 7.0047
SEG-LUN-P41 PHASE II PILOT STUDY OF PALA CHEMOTHERAPY FOR ADVANCED BRONCHOGENIC CARCINOMA 7.0048
SEG-76LUN0203 PHASE III ADJUVANT IMMUNOTHERAPY WITH C. PARVUM AND LEVAMISOLE AND RADIOTHERAPY FOR INOPERABLE LUNG CARCINOMA 7.0049
SEG-77PLUN0302 PILOT PHASE II STUDY OF CAP (CYCLOPHOSPHAMIDE/ADRIAMYCIN/CIS-PLATINUM) FOR ADENOCARCINOMA OF THE LUNG 7.0050
SEG-78LUN326R PHASE III CAMF VS CAP-I VS CTX/ADR THERAPY FOR ADVANCED SQUAMOUS, LARGE CELL OR ADENOCARCINOMA OF THE LUNG 7.0051
SWOG-8012 PHASE III CHEMOTHERAPY WITH FOMI (5-FU/VCR/MITO) VS CAP (CTX/ADR/CACP) VS FOMI/CAP FOR ADVANCED ADENO- AND LARGE CELL CARCINOMA OF THE LUNG 7.0052
SWOG-8015 PHASE III COMBINATION CHEMOTHERAPY WITH ADR/CACP VS ADR/CACP/VP-16 FOR SQUAMOUS CELL LUNG CARCINOMA 7.0053
SWOG-8068 PHASE I-II EVALUATION OF LUNG AND WHOLE BRAIN RADIOTHERAPY PLUS CHEMOTHERAPY (5-FU/MITO/VCR) FOR LIMITED ADENO AND LARGE CELL LUNG CARCINOMA 7.0054
BCRP-7708 PHASE II CHEMOTHERAPY WITH MAYTANSINE FOR SQUAMOUS CELL CARCINOMA OF THE LUNG 7.0055
BCRP-7713 CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE AND DIMETHYLSULFOXIDE FOR METASTATIC EPIDERMOID CARCINOMA OF THE LUNG 7.0056
BCRP-7819 CYCLOPHOSPHAMIDE PLUS WHOLE-BODY HYPERTHERMIA FOR ADENOCARCINOMA AND LARGE CELL CARCINOMA OF THE LUNG 7.0057
BCRP-7907 COMBINATION CHEMOTHERAPY WITH CTX/ADR/VP-16 WITH AND WITHOUT CACP FOR ADVANCED NON-SMALL CELL CANCER OF THE LUNG 7.0058
BCRP-7915 DAVA WITH AND WITHOUT CIS-PLATINUM FOR ADVANCED NON-SMALL CELL CARCINOMA OF THE LUNG 7.0059
LCSG-772 ADJUVANT BCG/INH/LEV IMMUNOTHERAPY VS CAP-I (CTX/ADR/CACP) FOR STAGE II AND III LARGE CELL AND ADENOCARCINOMA OF THE LUNG 7.0060

LCSG-773	ADJUVANT RADIOTHERAPY WITH OR WITHOUT LEVAMISOLE IMMUNOTHERAPY FOR EPIDERMOID CARCINOMA OF THE LUNG, STAGES II AND III	7.0061
LCSG-791	CAP-I CHEMOTHERAPY VS RADIOTHERAPY VS BOTH MODALITIES FOR PARTIALLY RESECTED LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER	7.0062
LCSG-801	COMBINATION CHEMOTHERAPY WITH CAP-I (CTX/ADR/CACP) VS NO THERAPY FOR COMPLETELY RESECTED NON-SMALL CELL LUNG CARCINOMA	7.0063
MAYO-782102	T-CAP (TZT/CTX/ADR/CACP) VS FAM (5-FU/ADR/MITO) COMBINATION CHEMOTHERAPY FOR ADENOCARCINOMA OF THE LUNG	7.0064
MAYO-792401	CAP-I (CTX/ADR/CACP) VS V-CAP-I (CTX/ADR/CACP/VP-16) VS T-CAP (CTX/ADR/CACP/TZT) PLUS RADIOTHERAPY FOR NONRESECTABLE NON-SMALL CELL LUNG CANCER	7.0065
MAYO-792407	CHEMOTHERAPY WITH CTX, ADR, CACP, MITO FOR ADVANCED NON-SMALL CELL LUNG CANCER	7.0066
MAYO-802501	PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED LUNG CANCER	7.0067
MAYO-802502	PHASE II CHEMOTHERAPY WITH DON FOR METASTATIC OR RECURRENT LUNG CANCER	7.0068
MDA-DT-7623	NUTRITIONAL SUPPORT FOR PATIENTS ON PROTOCOL MDAR-102 CHEMOTHERAPY AND IMMUNOTHERAPY FOR METASTATIC LUNG CARCINOMA	7.0069
MDAR-328	PHASE II CHEMOTHERAPY WITH PALA, BRUCEANTIN OR VINDESINE FOR NON-OAT CELL LUNG CANCER	7.0070
MDAR-335	CAP-1 (CYCLOPHOSPHAMIDE/ADRIAMYCIN/CIS-PLATINUM) CHEMOTHERAPY PLUS RADIOTHERAPY FOR NON-OAT CELL LUNG CANCER	7.0071
MDAR-339	COMBINATION CHEMOTHERAPY WITH FAM (5-FLUOROURACIL/ADRIAMYCIN/MITOMYCIN-C) FOR NONRESECTABLE ADENOCARCINOMA OF THE LUNG	7.0072
MDAR-385	PHASE II CHEMOTHERAPY WITH PCNU FOR METASTATIC LUNG CANCER OF ALL TYPES REFRACTORY TO FIRST LINE CHEMOTHERAPY	7.0073
MDAR-386	RADIOTHERAPY PLUS COMBINATION CHEMOTHERAPY WITH CEP (CTX/VP-16/CACP) VS CAP (CTX/ADR/CACP) FOR LIMITED NON-OAT CELL LUNG CANCER	7.0074
MDAR-402	PHASE II COMBINATION CHEMOTHERAPY WITH CACP/VP-16 FOR EXTENSIVE NON-OAT CELL LUNG CANCER	7.0075
MDAR-405	PHASE II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR METASTATIC LUNG CANCER	7.0076
MSKCC-7952	PHASE II EVALUATION OF HUMAN LEUKOCYTE INTERFERON IN ADVANCED NON-SMALL CELL LUNG CANCER	7.0077
MSKCC-8017	DAVA/CACP/BLEO COMBINATION CHEMOTHERAPY VS METHYL-GAG SINGLE-AGENT CHEMOTHERAPY FOR NON-SMALL CELL LUNG CANCER	7.0078
MTS-9	METHOTREXATE/ADRIAMYCIN/CYCLOPHOSPHAMIDE/CCNU WITH OR WITHOUT C. PARVUM OR LEVAMISOLE FOR PRIMARY LUNG CANCER	7.0079
NCI-78-C-19	SEQUENTIAL CMC (CTX/MTX/CCNU) AND VAP (VCR/ADR/PCB) WITH/WITHOUT RADIOTHERAPY AND WITH/WITHOUT THYMOSIN IN LIMITED LUNG CARCINOMA	7.0080
WSU-C-27678	PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED CARCINOMA OF THE LUNG	7.0081
WSU-C-30579	PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED CANCER OF THE LUNG	7.0082
WSU-C-35580	PHASE II CHEMOTHERAPY WITH PCNU FOR ADVANCED LUNG CARCINOMA	7.0083
CA-LUN-1	PHASE III STUDY OF CHEMOTHERAPY WITH ADR/CCNU/HMM/MTX AND AMPHOTERICIN B IN ADVANCED LUNG CANCER	7.0084
IL-LUN-1	BCG IMMUNOTHERAPY ADJUVANT TO RADIOTHERAPY FOR INOPERABLE BRONCHOGENIC CARCINOMA WITHOUT DISTANT METASTASES	7.0085
IL-LUN-3	COMPARISON OF CHEST WALL AND ARM VACCINATION WITH BCG FOR BRONCHOGENIC CARCINOMA	7.0086

MI-LUN-1 IMMUNOTHERAPY WITH BCG FOR LUNG CANCER STAGES I THROUGH III 7.0087

NC-LUN-2 NONSPECIFIC IMMUNOSTIMULATION WITH BCG IN TREATMENT OF BRONCHOGENIC CANCER 7.0088

NY-LUN-1 IMMUNOTHERAPY WITH BCG FOR PRIMARY RESECTABLE NON-OAT CELL LUNG CANCER 7.0089

OH-LUN-1 ADJUVANT IMMUNOTHERAPY WITH BCG OR BCG PLUS NEURAMINIDASE-TREATED TUMOR CELLS FOR RESECTED LUNG CANCER 7.0090

PA-MSHMC-LUN-1 ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE FOR NON-SMALL CELL LUNG CANCER 7.0091

RPMI-PPC-445 ADJUVANT TUMOR SPECIFIC ACTIVE IMMUNOTHERAPY OF SQUAMOUS CELL CARCINOMA OF THE LUNG 7.0092

WA-LUN-1 SURGERY AND ADJUVANT IMMUNOTHERAPY WITH BCG AND LEVAMISOLE FOR COMPLETELY RESECTED NON-SMALL CELL CANCER OF THE LUNG 7.0093

YALE-L-1 IMMUNOTHERAPY WITH INTRATUMORAL BCG PRIOR TO SURGERY FOR CARCINOMA OF THE LUNG 7.0094

CAN-NCIC-BR2 ADJUVANT IMMUNOTHERAPY WITH FREUND'S COMPLETE ADJUVANT (FCA) OR FCA/TUMOR ANTIGEN FOR BRONCHOGENIC CARCINOMA 7.0095

CHILE-LUN-1 COMBINATION CHEMOTHERAPY WITH VCR/ADR/CTX/CACP/CCNU VS ADR/CTX/CACP FOR ADVANCED BRONCHOGENIC CANCERS 7.0096

EORTC-08742 RADIOTHERAPY ALONE OR WITH CTX/MTX/CCNU CHEMOTHERAPY AND/OR BCG IMMUNOTHERAPY FOR LUNG CANCER 7.0097

EORTC-08743 RADIOTHERAPY PLUS CHEMOTHERAPY WITH CTX, VCR, MECCNU, BLEO, ADR, MTX, PLUS HMM FOR UNDIFFERENTIATED BRONCHOGENIC CARCINOMA 7.0098

EORTC-73009 CHEMOTHERAPY WITH CTX VS CTX/DEHYDROEMETINE FOR EVALUABLE CARCINOMA OF THE LUNG 7.0099

FRE-PAR-CPB-0177 IMMUNOTHERAPY WITH MYCOBACTERIUM SMEGMATIS ATCC 607 AS ADJUVANT THERAPY TO SURGERY IN PRIMARY BRONCHOGENIC CARCINOMA 7.0100

ITA-MIL-LC791 ADJUVANT THERAPY WITH VP-16213 VS PLACEBO FOR NON-OAT CELL BRONCHOGENIC CARCINOMA 7.0101

ITA-MIL-LC792 COMBINATION CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE (CTX)/HEXAMETHYLMELAMINE (HMM) VS CTX/VP-16213 FOR INOPERABLE NON-OAT CELL LUNG CANCER 7.0102

JAP-NCCH-L-1 CHEMOTHERAPY WITH CTX PLUS LONG-TERM VS SHORT-TERM BCG IMMUNOTHERAPY ADJUVANT TO SURGERY IN STAGE I LUNG CANCER 7.0103

SECTION 7

LUNG TUMORS

7A. SMALL CELL (OAT CELL) LUNG TUMORS

7.0001 PHASE III MTX, ADR, CCNU, CTX, VCR CHEMOTHERAPY IN TWO COMBINATIONS PLUS RADIOTHERAPY AND MER IMMUNOTHERAPY FOR OAT CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) CLB-7781

OBJECTIVES:

I. Test whether chemotherapy with either of two combinations: MACC - methotrexate (MTX)/adriamycin (ADR)/CCNU/cyclophosphamide (CTX) vs. CCV-AV - CCNU/CTX/Vincristine (VCR) alternating with ADR/VCR - and radiotherapy to the primary site and brain, produce a higher frequency of response (complete or partial) or longer durations of response, affect patterns of relapse, or prolong survival in patients with localized small cell (oat cell) carcinoma of the lung, as compared to historical controls.

II. Test whether the two combinations used with radiotherapy have significantly different effects on those parameters.

III. Test whether immunotherapy with MER (methanol extraction residue of Bacillus Calmette-Guerin), added to combination chemotherapy (with either of two regimens) significantly affects these same parameters in patients initially responsive to combination chemotherapy and radiotherapy.

IV. Evaluate psychosocial function in patients with localized small cell carcinoma of the lung before, during and after treatment, using: the rating of psychosocial function; the handicap rating scales; the profile of mood states; and demographic data.

PROTOCOL ENTRY CRITERIA: Patients previously untreated except by surgery, with histologic proof of localized small cell, undifferentiated (oat cell) carcinoma of the bronchus according to the World Health Organization criteria as modified by Mary Matthews. Patients must have a creatinine clearance of at least 50 ml/min, an estimated life expectancy greater than one month, a performance status of less than 4, and adequate cardiac status.

PROTOCOL OUTLINE: Randomized study.

Arm I: Induction. 4-Drug Combination Chemotherapy plus Radiotherapy. MACC: Methotrexate, MTX, NSC-740; Adriamycin, ADR, NSC-123127; CCNU, NSC-79037; Cyclophosphamide, CTX, NSC-26271. Megavoltage (1 MeV or greater) Radiotherapy.

Arm II: Induction. Alternating Chemotherapy plus Radiotherapy. 3-Drug Combination Chemotherapy. CTX; CCNU; VCR. Alternating with: 2-Drug Combination Chemotherapy. ADR; VCR, plus Radiotherapy, as in Arm I.

Following Induction, reassess all patients as to response achieved and performance status. Separately rerandomize Arm I and Arm II responders into one of two Maintenance Arms.

Maintenance:

Arm III: Continuation of Induction Chemotherapy: MACC or CCV-AV.

Arm IV: Continuation of Induction Chemotherapy plus Immunotherapy. MACC or CCV-AV, plus MER-BCG, MER, NSC-143769.

STRATIFICATION BY: Participating institutions, localized vs. disseminated disease (the latter are assigned to Protocol CLB-7782).

SPECIAL STUDY PARAMETERS: Deep tendon reflexes and estimates of muscle strength; liver and renal function tests; bone marrow biopsy; liver, bone and brain scans; skin tests; psychological tests; demographic data; pulmonary function studies prior to radiotherapy (Addendum #3, December 1978).

END POINTS: Response/remission rate, survival time, survival rate, duration of response, relapse patterns, psychosocial changes.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction: Give all dosages on the first day of each 3-week course.

Arm I: Give two courses of MACC before (on days 1 and 21) and two after Radiotherapy (on days 84 and 105): MTX - 30 mg/sqm iv; ADR - 35 mg/sqm iv, omit on day 84; CCNU - 30 mg/sqm po; CTX - 400 mg/sqm iv; plus 2500 rads in 10 treatments over 2 weeks beginning on day 42. After a two week rest period, give an additional 2000 rads in a 10 day period. In addition, deliver 3000 rads to the whole brain in 10 treatments beginning on day 42. Limit dose to spinal cord to 4300 rad (Addendum 3).

Arm II: Give one course of CCV-AV before and one after Radiotherapy. CTX - 700 mg/sqm iv on days 1 and 84; CCNU - 70 mg/sqm po on days 1 and 84; VCR - 1.0 mg/sqm (2.0 mg maximum) iv on days 1, 21, 84 and 105; ADR - 50 mg/sqm iv on day 21 and 105. Begin Radiotherapy as in Arm I on day 42. At day 136 reassess and restage all patients. Remove patients with disease progression from study. Rerandomize responders to Maintenance.

Maintenance:

Arm III: A. Enter patients induced on Arm I. MTX, CTX, CCNU as in Arm I q 21 days, days 136 through 304, then q 56 days, days 360 through 696, plus ADR - q 21 days, days 136 through 283 only. B. Enter patients induced on Arm II: CTX, CCNU as in Arm II, q 42 days, days 136 through 304, then q 112 days, days 416 through 640; VCR -as in Arm II, q 21 days, days 136 through 304, then q 56 days, days 360 through 695; ADR as in Arm II, q 42 days, days 157 through 283.

Arm IV: A. Enter patients induced on Arm I. MACC as in Arm IIIA, plus MER - 200 micrograms id into each of 3 sites on the anterior body surface, each site being drained by a different set of lymph nodes, which have not been excised or irradiated. In addition, inject doses of 200, 100, 10, 1.0 and 0.1 and 0.01 micrograms in a linear array of sites on an interior thigh. Observe these sites in 1-3 weeks and use the smallest dose of MER which produced areas of induration 1 cm in diameter with minimal or no central necrosis for subsequent courses of treatment with MER. Inject all subsequent doses at these sites but at least 1 cm distant from the previous injection in the same area. Administer MER q 6 weeks, days 136-304, and q 8 weeks, day 360-696. B. For patients induced on Arm II: CCV-AV, as in Arm II, plus MER Immunotherapy, as in Arm IVA. Patients who demonstrate complete or partial response or whose disease is stable within 2 months of therapy will continue treatment until day 696 or until the development of prohibitive drug toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CCNU - 10, 40 and 100 mg capsules; MTX - 50 mg vials; CTX - 500 mg vials; VCR - 1 and 5 mg ampules; MER - 1 mg/ml suspension.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 01001078

7.0002 PHASE III COMBINATION CHEMOTHERAPY WITH MACC VS MACC PLUS RADIOTHERAPY VS CCV-AV FOR EXTENSIVE SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) CLB-7782

OBJECTIVES:

I. Test whether the alternating combination CCV-AV; CCNU, cyclophosphamide (CTX), vincristine (VCR) - adriamycin (ADR), VCR will prolong the disease control interval as measured from the start of protocol to the first documented disease progression or recurrence when compared with continuous MACC: methotrexate (MTX), ADR, CCNU, CTX. Compare these two programs also with respect to objective response frequencies, remission duration, and survival.

II. Test whether the addition of irradiation to the primary lesion and draining lymph nodes in conjunction with MACC will prolong the disease control interval when compared with the continuous MACC program. Compare these two programs also with respect to objective response frequencies, remission duration, relapse patterns, and survival.

III. Evaluate psychosocial function in patients with localized small cell carcinoma of the lung before, during, and after treatment, using the rating of psychosocial function, the handicap rating scale, the profile of mood states, and demographic data.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age previously untreated except by surgery with measurable, small cell anaplastic carcinoma of the lung histologically confirmed according to the Working Party for Lung Cancer Criteria. Patients must have clinically demonstrable disease outside of one hemithorax and the ipsilateral supraclavicle nodes. They must have adequate blood counts and cardiac, renal and hepatic functions.

PROTOCOL OUTLINE: Randomized study.

Arm I: Concurrent 4-Drug Combination Chemotherapy plus Radiotherapy. MACC: Methotrexate, MTX, NSC-740; Adriamycin, ADR, NSC-123127; CCNU, NSC-79037; Cyclophosphamide, CTX, NSC-26271; plus megavoltage radiotherapy.

Arm II: Concurrent 4-Drug Combination Chemotherapy. MACC - as in Arm I.

Arm III: Alternating 2- and 3-Drug Combination Chemotherapies. CCV-AV: CTX; CCNU; Vincristine, VCR, NSC-67574, alternating with ADR; VCR.

STRATIFICATION BY: Participating institutions, performance status: good risk - 0 or 1, poor risk - 2 or 3.

SPECIAL STUDY PARAMETERS: Liver and renal function tests; bone marrow studies; liver, bone and brain scans; evaluation of psychosocial function; ECHO.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival, relapse pattern.

CURRENT STATUS: 270 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Arm I: MACC: MTX - 30 mg/sqm iv on day 1; ADR - 40 mg/sqm (maximum dose 450 mg/sqm) iv on day 1; CCNU - 30 mg/sqm po on day 1; CTX - 400 mg/sqm iv on day 1. Repeat course q 3 weeks for at least 4 courses - 2 before radiotherapy and 2 starting 1 week after the completion of radiotherapy. Omit ADR from the 3rd cycle of MACC. When the maximum dose of ADR has been given continue MTX, CCNU and CTX q 3 weeks until relapse. Radiotherapy - 3000 rads given in 12 days starting on day 42 to the primary disease site, the whole width of the mediastinum extending superiorly above the supersternal notch and inferiorly 4 cm below the carina.

Arm II: 4-Drug Combination Chemotherapy. MACC, as in Arm I.

Arm III: CCNU - 70 mg/sqm po on days 0, 84; CTX - 700 mg/sqm iv on days 0, 21, 84, 105; VCR - 2.0 mg iv on days 0, 21, 42, 63, 84, 105; ADR - 75 mg/sqm iv on days 42, 63. Repeat course q 84 days, with ADR beginning on day 42.

Remove from study patients with non-CNS disease progression after 2 courses of therapy and follow for survival. Continue therapy for all other patients until prohibitive drug toxicity or tumor progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00861078

7.0003 PHASE II CHEMOTHERAPY WITH MGBG FOR REFRACTORY SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) CLB-8073

OBJECTIVES:

I. Determine CR and PR frequency, duration of response, and survival of patients treated with methylglyoxal bis-guanylhydrazone (MGBG).

II. Determine the frequency of regression, duration of regression, and survival of patients with evaluable but not clearly measurable disease treated with MGBG.

III. Provide further clinical and laboratory data regarding the toxicity of MGBG.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented, measurable or evaluable, locally advanced and/or metastatic oat cell carcinoma of the lung using World Health Organization criteria. Patients must have been previously treated with combination chemotherapy with or without radiotherapy and have demonstrated clear progression or relapse of disease. Patients who have had additional therapy after failure on first line combination chemotherapy are eligible if there is clear progression or relapse. Four weeks must have elapsed from prior radiotherapy. Patients must have adequate renal and hematologic parameters, a performance status of 3 or less, and must be older than 16 years.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methylglyoxal bis-guanylhydrazone, Methyl-GAG, MGBG, NSC-32946.

STRATIFICATION BY: Presence of edema, ascites, or effusions.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Objective tumor response, response/remission rate, duration of response, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: 25-30 patients will be entered during 6-9 months.

DOSAGE SCHEDULE:

MGBG - 650 mg/sqm iv infusion over 45 minutes q week. Escalate dose by 50 mg/sqm at 3-week intervals until intolerable toxicity is experienced. Continue treatment at the highest tolerable dose until progressive disease appears. Start patients with edema, ascites, or effusions at 500 mg/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MGBG - 1.0 g vials.

DATE SUMMARIZED: 06/80

7.0004 PHASE II HIGH-DOSE INDUCTION CHEMOTHERAPY WITH CTX/MTX/VP-16 FOR DISSEMINATED SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) EST-PC-579

OBJECTIVES:

I. Determine the response rate and the toxicity of induction with high-dose cyclophosphamide/methotrexate/VP-16 in patients with extensive small cell bronchogenic carcinoma.

II. Evaluate this regimen for a future protocol for disseminated disease.

III. Evaluate this regimen for possible combination with radiotherapy in a future protocol for limited disease.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven extensive small cell bronchogenic carcinoma who have not received radiotherapy or chemotherapy. Patients must be under the age of 75 years and may have neither active infections nor brain metastases. Patients must have measurable or evaluable disease, adequate bone marrow and renal function, and a performance status of 0-2. There may be no history of another primary malignancy, except for skin cancer.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, chest x-ray, bone scan, brain scan, liver scan, bone marrow biopsy, bone survey.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 20 patients will be entered.

DOSAGE SCHEDULE:

Induction: CTX - 1500 mg/sqm iv on days 1 and 22; VP-16 - 60 mg/sqm iv on days 1 through 5 and 22 through 26; MTX - 15 mg/sqm po on days 8, 11, 15, 18, 29, 32, 36, and 39.

Maintenance: CTX - 500 mg/sqm iv on day 1; VP-16 - 60 mg/sqm iv on days 1, 3, and 5; MTX - 10 mg/sqm po on days 8, 11, 15, and 18. Begin after 6 weeks of Induction, and repeat q 3 weeks for 52 weeks.

All patients receive at least Induction. Patients who have not progressed after Induction will continue on Maintenance until progression. Patients in CR at the end of 52 weeks should have the remission documented by diagnostic procedures.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 200 and 500 mg vials; MTX - 50 mg vials; VP-16 - 100 mg ampules.

DATE SUMMARIZED: 12/80

7.0005 PHASE III STANDARD-DOSE CCM (CTX/CCNU/MTX) VS HIGH-DOSE CCM WITH OR WITHOUT AVP MAINTENANCE FOR SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) EST-1578

OBJECTIVES:

I. Compare the effect of standard-dose vs. high-dose CCM - cyclophosphamide (CTX)/CCNU/methotrexate (MTX) - for Induction and CCM with vs. without AVP - adriamycin (ADR)/vincristine (VCR)/procarbazine (PCB) - for Maintenance.

PROTOCOL ENTRY CRITERIA: Patients under 71 years of age with measurable or evaluable disease of histologically confirmed, small cell carcinoma (including oat cell) of the lung who have adequate renal and bone marrow function and a performance status less than 3. Patients must not have had prior chemotherapy or radiotherapy, active or prior second primary cancer, or cardiac problems.

PROTOCOL OUTLINE: Randomized study for Induction only. Randomize patients to Arm I, II or III, enter to Maintenance as indicated.

Arm I: Induction: 3-Drug Combination Chemotherapy. CCM: Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037; Methotrexate, MTX, NSC-740. Maintenance: 3-Drug Combination Chemotherapy alternating with 3-Drug Combination Chemotherapy. AVP: Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; alternating with CCM.

Arm II: Induction and Maintenance: 3-Drug Combination Chemotherapy. CCM, with high doses for Induction.

Arm III: Induction: 3-Drug Combination Chemotherapy. High-dose CCM. Maintenance: 3-Drug Combination Chemotherapy alternating with 3-Drug Combination Chemotherapy. AVP alternating with CCM.

STRATIFICATION BY: Participating institutions; performance status: 0 or 1 vs. 2; extent of disease: limited vs. extensive.

SPECIAL STUDY PARAMETERS: SMA-6 and 12, bone scan and survey, brain and liver scan, bone marrow biopsy.

END POINTS: Survival rate, objective tumor response, response/remission rate, duration of response, time to progression, survival time.

CURRENT STATUS: 350 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Induction:

Arm I: Induction: CTX - 700 mg/sqm iv on days 1 and 22; CCNU - 70 mg/sqm po on day 1; MTX - 15 mg/sqm po twice a week in weeks 2, 3, 5 and 6. Remove from study patients with no change or disease progression after 6 weeks. Maintenance: Enter responders as soon as blood counts are adequate. 1st 6 weeks: AVP: ADR - 60 mg/sqm (maximum dose 500 mg/sqm) iv on days 1 and 22; VCR - 1.4 mg/sqm (maximum dose 2.0 mg) iv on days 1 and 22; PBC - 50 mg/sqm po on day 1, 100 mg on day 2 and 200 mg (maximum dose) on day 3 and thereafter on days 4 through 10 and 22 through 23. 2nd 6 weeks: CCM: CTX - 500 mg/sqm iv on days 1 and 22; CCNU - 50 mg/sqm po on day 1; MTX - 10 mg/sqm po twice a week in weeks 2, 3, 5 and 6. Continue alternating AVP/CCM therapy until maximum dose of ADR has been given, then continue CCM therapy alone.

Arm II: Induction: CCM: CTX - 1500 mg/sqm iv on days 1 and 22; CCNU, MTX, as in Arm I Induction. Evaluate on day 43 and remove nonresponders and patients with no change from study. Enter complete (CR) or partial responders (PR) to Maintenance: CCM, as in 2nd 6 weeks of Arm I Induction.

Arm III: Induction: CCM, as in Arm II Induction. Maintenance: AVP/C CM alternating therapy as in Arm I Maintenance.

Repeat therapy q 6 weeks until disease progression. Discontinue Chemotherapy in patients with confirmed, complete remission at 96 weeks. Follow up patients for survival and time to progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 200 and 500 mg vials; CCNU - 10, 40 and 100 mg capsules; ADR - 10 or 50 mg vials; VCR - 1 and 5 mg vials; MTX - 50 mg vials; PCB - 50 mg capsules.

DATE SUMMARIZED: 10/78

7.0006 PHASE III CHEMOTHERAPY WITH PALA, AMSA, VM-26, AND NCS AS SINGLE AGENTS IN SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) EST-2579

OBJECTIVES:

I. Screen N-(phosphonoacetyl)-L-aspartate (PALA), m-AMSA, VM-26, and neocarzinostatin for activity against advanced small cell lung carcinoma in patients resistant to standard chemotherapeutic agents.

PROTOCOL ENTRY CRITERIA: Patients with advanced, histologically proven small cell bronchogenic carcinoma resistant to standard chemotherapy. Patients must have measurable or evaluable disease, a performance status of 0 to 2, and adequate marrow, kidney, and liver functions. There should have been no prior chemotherapy with any of the protocol agents, and patients should be at least 3 weeks post chemotherapy (6 weeks for nitrosoureas). Patients may not have had prior radiotherapy to present areas of measurable or evaluable disease unless progression in these areas has occurred in the interim. Patients may not have brain metastases.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. N-(Phosphonoacetyl)-L-aspartate, PALA, NSC-224131.

Arm II: Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

Arm III: Single-agent Chemotherapy. VM-26, NSC-122819.

Arm IV: Single-agent Chemotherapy. Neocarzinostatin, NCS, NSC-157365.

STRATIFICATION BY: Participating institutions, performance status (0-1 vs. 2), extent of disease (limited vs. extensive).

SPECIAL STUDY PARAMETERS: Tumor measurement, hematologic parameters, liver and kidney function tests, chest x-rays, creatinine clearance prior to each NCS course.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, survival rate.

CURRENT STATUS: About 20 patients will be entered onto each arm in 1 year.

DOSAGE SCHEDULE:

Arm I: PALA - 5 g/sqm iv infusion q 14 days for a minimum of 2 doses. Patients with progressive disease after 2 doses may be removed from study; responders and those with stable disease will continue on study until evidence of progressive disease.

Arm II: AMSA - 120 mg/sqm iv q 3 weeks for a minimum of 2 doses. Patients with progressive disease after 6 weeks will go off study, while responders and those with stable disease will continue on treatment until progressive disease is encountered.

Arm III: VM-26 - 100 mg/sqm iv infusion q 7 days for a minimum of 4 weeks. Patients with progressive disease after 4 weeks will go off study, while others will continue on treatment until disease progression or the development of prohibitive toxicity.

Arm IV: NCS - 2 mg/sqm iv daily for 5 days q 4 weeks. After one course of therapy, patients with progressive disease will be taken off study and responders and those with stable disease will continue until progressive disease or prohibitive toxicity occurs.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 1 g ampules; AMSA - 75 mg ampules; VM-26 - 50 mg ampules; NCS - 2 mg unit vials.

DATE SUMMARIZED: 05/80

7.0007 PHASE III CHEMOTHERAPY WITH VP-16/ADR/MTX, CTX/CCNU/VCR/PCB PLUS RADIOTHERAPY FOR UNDIFFERENTIATED SMALL CELL ANAPLASTIC LUNG CANCER

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PROTOCOL NUMBER(S) NCOG-2O61

OBJECTIVES:

I. Assess effectiveness of chemotherapy with VAM: VP-16213 (VP-16)/adriamycin (ADR)/methotrexate (MTX), followed by radiotherapy and subsequent chemotherapy with alternating courses of VAM and POCC: cyclophosphamide (CTX)/CCNU/vincristine (VCR)/procarbazine (PCB), vs. chemotherapy with POCC only before and after radiotherapy for small cell anaplastic lung cancer.

PROTOCOL ENTRY CRITERIA: Patients less than 70 years of age with microscopically demonstrated, undifferentiated/anaplastic, small cell carcinoma who have a Karnofsky performance status 20% or better. Patients must be free of previous chemotherapy, previous radiotherapy, malignancy in previous 10 years, and/or medical contraindications for aggressive treatment.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy followed by Radiotherapy followed by alternating cycles of 3-Drug and 4-Drug Combination Chemotherapy. VAM: VP-16213, VP-16, NSC-141540; Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740; followed by megavoltage cranial irradiation; followed by alternating cycles of VAM and POCC: Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213.

Arm II: 4-Drug Combination Chemotherapy plus Radiotherapy. POCC; followed by Radiotherapy as in Arm I; followed by POCC.

STRATIFICATION BY: Participating institutions; extent of disease: regional or limited vs. extensive; Karnofsky performance status: 20 to 40% vs. 50 to 70% vs. 80 to 100%; prior emergency Radiotherapy; histology: oat/lymphocytic-like vs. polygonal/fusiform.

SPECIAL STUDY PARAMETERS: Pulmonary function, liver and kidney function, calcium, bone marrow biopsy, bone scan and x-ray, liver size and scan, adenopathy, brain scan.

END POINTS: Objective tumor response, overall disease activity, survival, time to progression, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: VAM: VP-16 - 200 mg/sqm iv infusion over 30 to 40 minutes; ADR - 50 mg/sqm (maximum cumulative dose 450 mg/sqm) iv; MTX - 30 mg/sqm iv. Repeat course on day 1 q 21 days. Follow with Radiotherapy: patients with extensive disease - 3000 rads midplane sagittal dose to whole brain in 2 weeks starting 1 week after initiation of cycle 3 of VAM; patients with limited disease - whole brain irradiation as above concurrent with thoracic irradiation of 5000 to 5500 rads in 5 to 7 weeks to site of primary tumor and bilateral mediastinal, hilar, and supraclavicular lymph nodes starting 3 weeks after initiation of cycle 3 of VAM. Do not exceed 4000 rads in 4 weeks to the spinal cord. Subsequent to irradiation, alternate POCC with VAM for 18 months or until progression of disease. POCC: CTX - 600 mg/sqm/day iv on days 1 and 8; CCNU - 60 mg/sqm po on day 1; VCR - 1.5 mg/sqm/day (maximum 2.0 mg) iv on days 1 and 8; PCB - 100 mg/sqm/day po on days 2 through 15. Repeat course q 28 days.

Arm II: Alternate POCC (2 cycles) as in Arm I with Radiotherapy as in Arm I for 18 months or until progression of disease. Start Radiotherapy in patients with extensive disease (whole brain only) 2 weeks after initiation of cycle 2 and for patients with limited disease (whole brain plus involved fields), 4 weeks after initiation of cycle 2.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules; VCR - 1 and 5 mg ampules; VP-16 - 100 mg ampules; CTX - 100 and 500 mg ampules; MTX - 5 and 50 mg vials; CCNU - 10, 40 and 100 mg capsules; PCB - 50 mg capsules in bottles containing 100.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 00280378

7.0008 PHASE III 7-DRUG VS 9-DRUG CHEMOTHERAPY IN EXTENSIVE DISEASE & LATE CONSOLIDATION RADIOTHERAPY IN LIMITED DISEASE SMALL CELL CARCINOMA

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PROTOCOL NUMBER(S) NCOG-2O91

OBJECTIVES:

I. Confirm the good results of NCOG Protocol #2061 in extensive small cell bronchogenic carcinoma using 7-drug chemotherapy with VAM (VP-16/adriamycin/methotrexate) and POCC (cyclophosphamide/CCNU/vincristine/procarbazine).

II. Test the value of early alternation of 7 drugs (POCC/VAM) vs. initial exposure to only VAM.

III. Test the effect of adding hexamethylmelamine plus cis-platinum to the 7-drug regimen in extensive-disease patients.

IV. Establish the response rate of POCC/VAM in patients with limited disease compared to the same therapy in extensive-disease patients.

V. Determine whether limited-disease patients with complete response after 5 cycles benefit from involved field radiation as consolidative therapy after 9 months of induction chemotherapy, compared to no further treatment.

PROTOCOL ENTRY CRITERIA: Patients with microscopically demonstrated undifferentiated/anaplastic small cell bronchogenic carcinoma who have not received previous chemotherapy. Limited-disease patients may not have received any prior radiotherapy, but extensive-disease patients may have received emergency radiotherapy. Patients must have a Karnofsky status of at least 30 percent and may not be older than 70 years. There must be no history of another malignancy except curable skin cancer within 10 years and no history of congestive heart failure or myocardial infarction within 5 years. Bone marrow, kidney, and liver function must be adequate.

PROTOCOL OUTLINE: Randomized study. Enter patients with extensive disease to Regimen A and those with limited disease to Regimen C.

Regimen A: 2-, 3-, and 4-Drug Alternating Combination Chemotherapy. Randomize patients to Arms I, II, and III.

Arm I: 3- and 4-Drug Alternating Combination Chemotherapy. VAM: VP-16213, VP-16, NSC-141540; Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740, alternating after 3 courses with POCC: Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213.

Arm II: 4- and 3-Drug Alternating Combination Chemotherapy. POCC: CTX/CCNU/VCR/PCB alternating with VAM: VP-16/ADR/MTX. Schedule varies from Arm I.

Arm III: 4-, 3-, and 2-Drug Alternating Combination Chemotherapy. POCC alternating with VAM alternating with HP: Hexamethylmelamine, HMM, NSC-13875; cis-Platinum, CACP, NSC-119875.

Regimen B: Whole Brain Irradiation. Megavoltage equipment with energy ranging from that of Co-60 to a maximum of 25 MeV photons. Enter all patients from Regimens A and C.

Regimen C: 4- and 3-Drug Alternating Combination Chemotherapy. POCC alternating with VAM.

Regimen D: Enter all CR and equivocal CR from Regimen C and randomize to Arms IV and V.

Arm IV: Involved Field Thoracic Radiation Therapy. Megavoltage equipment as in Regimen B.

Arm V: No further treatment.

STRATIFICATION BY: Participating institutions, Karnofsky performance status (80-100 vs. 50-70 vs. 30-40), prior emergency radiation therapy (yes vs. no, patients with extensive disease only).

SPECIAL STUDY PARAMETERS: Bone marrow biopsy, brain scan, bone x-rays, liver scan, brain scan or CT brain scan, chest x-ray, hematologic parameters, liver and kidney function tests.

END POINTS: Response/remission rate, time to response, disease-free interval, survival, performance status, toxicities.

CURRENT STATUS: Between 96 and 102 patients are expected to be accrued per year; of these approximately one-third will have limited disease.

DOSAGE SCHEDULE:

Arm I: VAM: VP-16 - 200 mg/sqm iv infusion over 30-40 minutes; ADR - 50 mg/sqm iv; MTX - 30 mg/sqm iv. Repeat courses at 3-week intervals for a total of 3 courses before alternating with POCC. POCC: CTX - 600 mg/sqm iv on days 1 and 8; CCNU - 60 mg/sqm po on day 1; VCR - 1.5 mg/sqm (maximum 2.0 mg) iv on days 1 and 8; PCB - 100 mg/sqm po on days 2 through 15. Alternate with VAM, starting VAM treatment 28 days after day 1 of POCC and POCC 21 days after day 1 of VAM. Continue for a total of 6 alternating courses of each combination.

Arm II: POCC alternating with VAM from the start of treatment for a total of 7 courses of each combination. Dosage as in Arm I.

Arm III: VAM and POCC as in Arm I. HP: CACP - 100 mg/sqm iv over 24 hours on day 1; HMM - 200 mg/sqm po on days 3 through 9. Begin treatment with POCC followed 28 days after day 1 with VAM, followed 21 days after day 1 with HP, followed in 21 days after day 1 of HP with the next cycle. Repeat for a total of 5 courses of each combination.

Restage responders after 1 year of treatment. CR will be followed without additional treatment; PR and SD will continue therapy until progression; PD will be treated at the option of the investigator.

Regimen B: 3000 rads midplane sagittal dose through opposing lateral fields using 5 fractions of 300 rads per week for a total of 10 treatments over a period not to exceed 19 days. Treatment to begin 9-10 weeks after the initiation of Chemotherapy. Extensive-disease patients with an intracranial mass may receive booster doses to this lesion at the discretion of the radiotherapist.

Regimen C: POCC alternating with VAM as in Arm II for a total of 5 courses of each combination. Restage responders at 9 months. CR will be stratified according to Karnofsky status and randomized to Arms IV and V; SD will continue therapy until progression, and PD will be treated at the discretion of the investigator.

Arm IV: 5500 rads to the treatment volume in 5-7 weeks at a dose rate of 900-1000 rads per week with fractions of 180-200 rads.

Arm V: No further treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules; VCR - 1 and 5 mg ampules; VP-16 - 100 mg ampules; CTX - 100 and 500 mg ampules; MTX - 5 and 50 mg vials; CCNU - 10, 40, and 100 mg capsules; PCB - 50 mg capsules; HMM - 50 and 100 mg capsules; CACP - 10 mg vials.

DATE SUMMARIZED: 07/80

7.0009 PHASE II PILOT CHEMOTHERAPY WITH VP-16/MTX/CF/CCNU FOR RECURRENT OR PROGRESSIVE OAT-CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) SEG-LUN-P32

OBJECTIVES:

I. Determine whether systemic treatment with a combination of VP-16213 (VP-16), methotrexate (MTX), and CCNU will result in tumor regression in patients who are either resistant to vincristine, adriamycin, and cyclophosphamide, or who have recurred after initial treatment with that regimen.

II. Determine the duration of response and the quality of life associated with treatment of patients by this regimen.

III. Determine the morbidity associated with myelosuppression attendant on this regimen.

PROTOCOL ENTRY CRITERIA: Patients with oat cell lung cancer who have failed to respond completely or have progressed after initial response to adriamycin/cyclophosphamide therapy. Patients must have a performance status of at least 50, adequate hematologic function, and a creatinine clearance of at least 70 ml/min. There must have been no prior therapy with the study agents.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. CCNU, NSC-79037; VP-16213, VP-16, NSC-141540; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Liver/spleen scan, liver function tests, renal function tests.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, duration of response, quality of life.

CURRENT STATUS: 14 to 25 patients will be entered.

DOSAGE SCHEDULE:

CCNU - 80 mg/sqm po on day 1 q 6 weeks; VP-16 - 100 mg/sqm iv on days 1 through 3 q 3 weeks; MTX - 50 mg/sqm iv on day 1, followed in 36 hours by CF - 5 mg po given q 6 hours for 6 doses, repeated on days 8, 22, and 29 of each 42-day course. Remove from study patients with tumor progression by 6 weeks or with unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CCNU - 40 and 100 mg capsules; VP-16 - 100 mg ampules; MTX - 50 mg ampules; CF - 5 mg tablets.

DATE SUMMARIZED: 05/79

7.0010 PHASE II INDUCTION WITH HIGH-DOSE CAV (CTX/ADR/VCR) VS CAV PLUS VP-16 AND CAV CONSOLIDATION FOR METASTATIC SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) SEG-78LUN252

OBJECTIVES:

I. Determine the response rate (especially complete response rate) of patients with metastatic small cell lung carcinoma to a combination of high-dose CAV: cyclophosphamide (CTX), adriamycin (ADR) and vincristine (VCR) as Induction therapy.

II. Determine the value of adding VP 16-213 (VP-16) to this combination given at a conventional dose schedule with respect to response rate.

III. Determine response duration and survival to the above chemotherapy when complete and good responders continue on chemotherapy with CAV at conventional doses.

PROTOCOL ENTRY CRITERIA: 'Good risk' patients with histologically proven, measurable, progressive lesions of extensive metastatic small cell carcinoma of the lung. Patients must not have had prior chemotherapy or radiotherapy and must have an adequate cardiac status, a Karnofsky performance status of 50 or above and bilirubin above 1.2.

PROTOCOL OUTLINE: Randomized study, for Induction only until alternate Consolidation treatments are developed.

Induction:

Arm I: 3-Drug Combination Chemotherapy. CAV: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574.

Arm II: 4-Drug Combination Chemotherapy. CTX, ADR, VCR, plus VP-16-213, VP-16, NSC-141540.

Consolidation:

3-Drug Combination Chemotherapy. CAV, as in Arm I, at lower dosage.

Prophylactic Brain Radiotherapy (Optional). Megavoltage irradiation (Co-60, MeV x-rays) with effective photon energies higher than 1 MeV.

STRATIFICATION BY: None.

SPECIAl STUDY PARAMETERS: Bone marrow aspiration and biopsy; LDH; liver, bone, and brain scans.

END POINTS: Response/remission rate, response duration, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 6 to 28 patients will be entered in 4 to 5 months.

DOSAGE SCHEDULE:

Induction:

Arm I: High-dose CAV: CTX - 1200 mg/sqm (maximum dose 2400 mg/dose) iv on day 1; ADR - 70 mg/sqm (maximum 140 mg/dose; maximum cumulative dose 450 mg/sqm) iv on day 1; VCR - 2 mg/sqm (maximum 2 mg/dose) iv on day 1. Repeat course on day 22 for a total of 2 courses.

Arm II: CTX - 1000 mg/sqm (maximum 2000 mg/dose) iv on day 1; ADR - 40 mg/sqm (maximum 8 mg/dose) VCR - 1 mg/sqm (maximum 2 mg/dose) iv on day 1; VP-16 - 100 mg/sqm iv on days 1, 2 and 3. Repeat course on day 22 for a total of 2 courses.

Evaluate patients in Arms I and II on day 43. Enter complete and good partial responders to Consolidation. Remove patients with lesser response from study.

Consolidation:

CAV - CTX - 600 mg/sqm (maximum 1200 mg/dose) iv on day 1; ADR - 60 mg/sqm (maximum 120 mg/dose) iv on day 1; VCR - 1.4 mg/sqm (maximum 2 mg dose) iv on day 1. Repeat course q 3 weeks for 5 more courses. Evaluate response 3 weeks after completion of Consolidation. Give no further therapy to complete responders until disease progression; treat patients with good partial responses at physician's discretion. Treat patients with CNS metastasis with Radiotherapy and steroids. Follow up all patients for survival.

Prophylactic Brain Radiotherapy: Enter responders between the 3rd and 4th course of Chemotherapy, then continue Consolidation of complete and good partial responders. 3000 rads given in 10 fractions over 14 days to the whole brain.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; ADR - 100 and 50 mg vials; VCR - 1 and 5 mg vials; VP-16 - 100 mg ampules.

DATE SUMMARIZED: 05/79

7.0011 PHASE III CTX/ADR/VCR THERAPY ALONE OR WITH RADIOTHERAPY FOLLOWED BY VP-16/HMM OR MTX/CF/VP-16/HMM FOR SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) SEG-78LUN328

OBJECTIVES:

I. Determine whether treatment of limited undifferentiated, small cell carcinoma of the lung by radiation therapy to primary tumor, regional lymph nodes and brain, together with the adjunctive use of a multi-drug combination (cyclophosphamide (CTX)/adriamycin (ADR)/and vincristine (VCR) when compared to the same regimen without radiation therapy to the primary: increases the objective response rate, the duration of remission or of survival, improves the quality of life during survival, decreases the incidence of distant organ metastasis (other than brain) and reduces local recurrence.

II. Determine whether Consolidation chemotherapy with VP-16/hexamethylmelamine (HMM) can convert some partial responders (or patients with stable disease) to complete responders and determine the total duration of disease-free survival as well as total survival after induction and consolidation chemotherapy.

III. Determine whether nonresponders to the above Induction treatment regimens will respond to a combination of high-dose methotrexate (MTX)/VP-16/HMM as secondary therapy.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with histologically or cytologically proven undifferentiated small cell carcinoma of the lung, localized to the thorax. Tumor may have been resected. Patients must have a performance status of 30 or better and no previous chemotherapy or radiotherapy to the thorax. Patients must not have a second primary tumor which is not controlled.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I or II. Enter responders to Consolidation, others to Reinduction.

Arm I: Induction. 3-Drug Combination Chemotherapy plus Prophylactic Brain Radiotherapy. CAV: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574.

Arm II: Induction. 3-Drug Combination Chemotherapy plus Radiotherapy to Primary Tumor and Brain. CTX, ADR, VCR.

Consolidation: 2-Drug Combination Chemotherapy plus Vitamin Therapy. VP-16, NSC-141540; Hexamethylmelamine, HMM, NSC-13875; Vitamin B-6, NSC-36225.

Reinduction: 4-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590; VP-16, HMM as in Arm III.

STRATIFICATION BY: Participating institutions; involvement of ipsilateral scalene or supraclavicular nodules; performance status: 80-100 vs. 30-70; diagnosis: biopsy vs. cytological diagnosis.

SPECIAL STUDY PARAMETERS: Liver, bone and brain scans; bronchoscopy; sputum cytology; bronchogram; chest tomogram.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, remission duration, survival duration, quality of survival, incidence of local or distant recurrences, survival rate.

CURRENT STATUS: 166 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Arm I: CAV: CTX - 1000 mg/sqm (maximum dose 2000 mg) iv on day 1; ADR - 40 mg/sqm (maximum dose 100 mg) iv on day 1; VCR - 1 mg/sqm (maximum dose 2 mg) iv on day 1 (also on days 7 and 14 in the first course only). Repeat course q 3 weeks for 6 courses. Radiotherapy -1200 rad per week to whole brain in weeks 5, 8 and 11. Evaluate at 3 to 5 weeks, nonresponders or patients developing metastases can cross over to Arm II but are considered off study. At end of 6 courses, enter partial and complete responders to Consolidation, enter all others to Reinduction.

Arm II: CTX, ADR, VCR and whole brain Radiotherapy as in Arm I. Radiotherapy to hilar, mediastinal and supraclavicular lymph nodes plus primary tumor - 1500 rad in weeks 5 and 8, 1000 rad in week 11. Evaluate at 3 to 5 weeks and at end of 6 courses. Remove patients with progressive disease after 3 to 5 weeks from study. After 6 courses enter nonresponders to Reinduction, all others to Consolidation.

Consolidation: VP-16 - 200 mg/sqm iv on days 1 and 8; HMM - 280 mg/sqm po on days 1 through 14; Vitamin B-6 - 150 mg/day po. Repeat q 28 days for 3 courses.

Reinduction: MVH: MTX - 1 gm/sqm iv on days 1 and 14; CF - 20 mg/sqm iv on days 2 and 15 (24 hours after MTX dose), then 10 mg po q 6 hours for 12 doses, plus hydration on days 2 and 3; VP-16 - 200 mg/sqm iv on days 1 and 14; HMM - 280 mg/sqm po on days 1 through 14. Repeat course q 28 days for 6 courses. Evaluate after the third course and remove nonresponders from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; ADR - 10 and 50 mg vials; VCR - 1 and 5 mg vials; CF - 3 and 50 mg vials and 5 mg tablets; VP-16 - 100 mg vials; HMM - 50 and 100 mg capsules; MTX - 1 gm vials.

DATE SUMMARIZED: 10/78

7.0012 PHASE II COMPARISON OF HIGH-DOSE CAV (CTX/ADR/VCR) VS CONVENTIONAL-DOSE CAV PLUS VP-16213 IN GOOD-RISK METASTATIC SMALL CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) SEG-79LUN252

OBJECTIVES:

I. Determine response rate of patients with metastatic small cell lung carcinoma to a combination of high-dose cyclophosphamide (CTX), adriamycin (ADR), and vincristine (VCR) as Induction therapy.

II. Determine the value of adding VP-16213 to a combination of CTX, ADR, and VCR at conventional dosages in Induction therapy of extensive small cell lung carcinoma.

III. Determine duration of response and survival to this therapy when complete and good responders continue on chemotherapy with these drugs at conventional dosages.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic small cell lung carcinoma with at least one measurable lesion who have experienced recent progression. Patients may not have had prior radiotherapy or chemotherapy and must have a Karnofsky performance status of at least 50. Patients with angina or congestive heart failure or with a myocardial infarction within the past 6 months are ineligible.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. High-dose CAV: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574.

Arm II: 4-Drug Combination Chemotherapy. CAV plus VP-16213. CTX; ADR; VCR; VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters; liver and kidney function tests; chest and other appropriate x-rays; EKG; liver, bone, and brain scans; CAT.

END POINTS: Response/remission rate, duration of response, survival, objective tumor response.

CURRENT STATUS: Up to 28 evaluable patients may be entered.

DOSAGE SCHEDULE:

Arm I: CAV: CTX - 1200 mg/sqm (maximum dose 2400 mg) iv on days 1 and 21; ADR - 70 mg/sqm (maximum dose 140 mg) iv on days 1 and 21; VCR - 1 mg/sqm (maximum dose 2 mg) iv on days 1 and 21.

Arm II: CTX - 1000 mg/sqm (maximum dose 1200 mg) iv on days 1 and 21; ADR - 40 mg/sqm (maximum dose 120 mg) iv on days 1 and 21; VCR - 1 mg/sqm (maximum dose 2 mg) iv on days 1 and 21; VP-16 - 100 mg/sqm iv on days 1, 2, 3, 21, 22, and 24.

Patients from either arm who are complete or good partial responders to 2 courses of Induction therapy will continue on lower-dose CAV combination Chemotherapy for an additional 5 courses at 3-week intervals: CTX - 600 mg/sqm (maximum dose 1200 mg) iv on day 1; ADR - 60 mg/sqm (maximum dose 120 mg) iv on day 1; VCR - 1.4 mg/sqm (maximum dose 2 mg) iv on day 1. In the absence of hematological toxicity CTX will be increased by 25 percent for each subsequent course.

Prophylactic brain radiotherapy is optional.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200, and 500 mg vials; VCR - 1 mg ampules; VP-16 - 100 mg ampules.

DATE SUMMARIZED: 05/80

7.0013 PHASE III VCR/MTX/VP-16 VS VCR/ADR/CTX OR BOTH PLUS CRANIAL RADIOTHERAPY FOR EXTENSIVE SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) SWOG-7828

OBJECTIVES:

I. Improve the complete response rate and long-term, disease-free survival of patients with extensive small cell carcinoma of the lung.

II. Define, qualitate and quantify the toxicity of each regimen employed.

III. Compare the efficacy of two non-crossresistant regimens (cell cycle specific vs. cell cycle nonspecific) during Induction.

IV. Determine whether administration of a second, non-crossresistant regimen in Consolidation can convert stable disease or partial response to a better quality of response.

V. Determine the effect of intentional, early alternation of non-crossresistant regimens on the complete response rate.

VI. Determine whether 'reinduction' at 24 and 52 weeks has a favorable effect on response duration and survival.

VII: Determine whether administration of intrathecal methotrexate at 'reinduction' can affect the incidence of nonbrain CNS relapse.

PROTOCOL ENTRY CRITERIA: Patients with extensive small cell undifferentiated carcinoma of the lung. Patients must have evidence of disease after surgery and/or radiotherapy and have had no prior brain radiation therapy nor chemotherapy. Patients must have adequate cardiac and renal function.

PROTOCOL OUTLINE: Induction is randomized. Consolidation is nonrandomized and all responding or stable patients enter Maintenance following Consolidation. Following Maintenance, patients are randomly assigned to Late Maintenance or Reinduction.

Induction. Randomize all patients to Arms I, II, or III.

Arm I: 3-Drug Combination Chemotherapy. VMV: Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; VP-16, NSC-141540.

Arm II: 3-Drug Combination Chemotherapy. VAC: VCR; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm III: 5-Drug Combination and Sequential Chemotherapy. VMV/VAC: VCR, MTX, VP-16, ADR, CTX.

Consolidation. Enter patients with complete response (CR) from Arm I and patients with partial response (PR) or stable disease (SD) from Arm II to Regimen A. Enter PR and SD from Arm I and CR from Arm II to Regimen B. Enter CP, PR, and SD from Arm III to Regimen C.

Regimen A: 2-Drug Combination Chemotherapy. MTX, VP-16.

Regimen B: 2-Drug Combination Chemotherapy. ADR, CTX.

Regimen C: 4-Drug Combination Chemotherapy. MTX, VP-16, ADR, CTX.

Maintenance. Enter all CR, PR, and SD from Consolidation Therapy. 2-Drug Combination Chemotherapy plus Prophylactic Radiotherapy. CTX, VP-16, plus Cobalt-60 or external beam generators with 2 to 6 MeV peak energy.

Late Maintenance. 2-Drug Combination Chemotherapy. CTX, VP-16.

Reinduction. Assign patients to Regimen D if Induction Therapy was in Arms I or III, to Regimen E if Induction Therapy was in Arm II.

Regimen D: 5-Drug Combination and Intrathecal Chemotherapy. VCR, MTX, VP-16, CTX, and Citrovorum factor, CF, NSC-3590.

Regimen E: 6-Drug Combination and Intrathecal Chemotherapy. VCR, ADR, CTX, MTX, CF, VP-16.

STRATIFICATION BY: Participating institutions; prior radiotherapy; performance status: fully ambulatory vs. less than fully ambulatory.

SPECIAL STUDY PARAMETERS: Bone, brain, and liver scan; IVP.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of response, disease-free interval, survival time.

CURRENT STATUS: 279 patients will be entered in 2.7 years.

DOSAGE SCHEDULE:

Induction.

Arm I: VMV: VCR - 2 mg iv on day 1. Repeat q 7 days for a total of 6 doses; MTX - 60 mg/sqm iv on days 1 and 22; VP-16 - 50 mg/sqm iv on days 1 through 5 and 22 through 26.

Arm II: VAC: VCR - as in Arm I; ADR - 60 mg/sqm iv on days 1 and 22; CTX - 1000 mg/sqm iv on days 1 and 22.

Arm III: VMV/VAC: VCR - as in Arm I; MTX - 60 mg/sqm iv on day 1; VP-16 - 50 mg/sqm iv on days 1 through 5; ADR - 60 mg/sqm iv on day 22; CTX - 1000 mg/sqm iv on day 22. Remove from study all patients with progressive disease following Induction.

Consolidation. On day 43 enter responders to regimens indicated.

Regimen A: MTX - 60 mg/sqm iv on days 43 and 64; VP-16 - 50 mg/sqm iv over 30 minutes on days 43-47 and 64-68.

Regimen B: ADR - 60 mg/sqm iv on days 43 and 64; CTX - 1000 mg/sqm iv on days 43 and 64.

Regimen C: MTX - 60 mg/sqm on day 43; VP-16 - 50 mg/sqm iv on days 43 through 47; ADR - 60 mg/sqm iv on day 64; CTX - 1000 mg/sqm iv on day 64. Remove from study all patients with progressive disease following Consolidation.

Maintenance. On day 85 enter all responders from Consolidation following clinical restaging. CTX - 750 mg/sqm on days 85, 113, and 141; VP-16 - 120 mg/sqm iv on days 85, 93, 113, 121, 141, and 149, plus 3000 rads given over a period of 2 weeks to the whole brain. Begin Radiotherapy for patients with evidence of brain metastases at study entry on day 1 of Induction, same dosage plus a boost of 900 rad given over 3 days to patients with isolated lesions, a boost of 600 rad given over 2 days to entire brain to all patients. In addition, give these patients Dexamethasone, NSC-34521, 16 mg/day po in 4 divided doses prior to irradiation until completion of course, then taper to discontinue over 4 weeks time.

Remove from study patients with progressive disease following Maintenance. Rerandomize all other patients to late Maintenance or Reinduction, following a second clinical restaging.

Late Maintenance. CTX, VP-16 - as in Maintenance. Begin on day 169 and repeat course q 4 weeks for a total of 11 Maintenance courses.

Reinduction. Enter patients on day 169 (week 24) to courses as indicated.

Regimen D: Enter patients induced on Arms I or III. VCR - 2 mg iv on days 1, 8, and 15; VP-16 - 50 mg/sqm iv on days 1 through 5; MTX - 60 mg/sqm iv on day 1 and 10 mg/sqm it on day 5; CF - 6 mg im or sc q 6 hours for 8 doses starting 24 hours after it MTX. Repeat course once beginning in week 52.

Repeat Maintenance courses: CTX on day 1, VP-16 on days 1 and 8 q 28 days beginning in week 28 for a total of 6 courses.

Regimen E: Enter patients induced on Arm II. VCR - as in Maintenance; ADR - 60 mg/sqm iv on day 1; CTX - 1000 mg/sqm iv on day 1; MTX - 10 mg/sqm it on day 1; CF - 6 mg im q 6 hours for 4 doses starting 24 hours after it MTX. Repeat course once beginning in week 52 and then enter patients to Maintenance, as in Regimen D.

Restage all patients after the final course of therapy (ending in week 54). Remove from study patients in CR. Continue patients in PR and SD on Maintenance, as in Regimen D for a total of 2 years or until disease progression. Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200, and 500 mg ampules; DM - 0.5, 0.75, 1.5, and 4.0 tablets; MTX - 50 mg vials; VCR -1 and 5 mg ampules; VP-16 - 100 mg vials; CF - 3 mg ampules.

DATE SUMMARIZED: 02/79

7.0014 PHASE III CHEMOTHERAPY WITH ADR/CTX/MTX/VCR/VP-16 PLUS RADIOTHERAPY FOR SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) SWOG-7924

OBJECTIVES:

I. Determine the efficacy of sequentially alternating, mutually noncross-resistant, multidrug regimens in remission Induction and Intensification therapy in patients with limited small cell lung carcinoma.

II. Determine the value of chest radiotherapy added to intensive system chemotherapy in reducing chest recurrences, and in improvement of survival.

III. Determine the relative efficacy and toxicity of low-dose, extensive chest radiation when used in close chronologic sequence with systemic multiagent chemotherapeutic regimens.

IV. Determine whether radiotherapy ports should set according to tumor size prior to or after Induction chemotherapy.

V. Determine the value of combined systemic chemotherapy and radiotherapy in the control of bulky chest disease.

PROTOCOL ENTRY CRITERIA: Patients with histologically or cytologically proven small cell carcinoma of the lung; sputum cytological diagnosis is acceptable. Disease must be limited, confined to 1 hemithorax, mediastinum, hilar and supraclavicular areas, which can be encompassed within a single radiation therapy port. Patients must have no prior chemotherapy or radiotherapy (except for the control of localized skin cancer). Patients may have had prior surgical diagnostic or therapeutic techniques but must have evidence of post-surgery disease. Patients must have no congestive heart failure; serum creatinine must be greater than 20 mg percent.

PROTOCOL OUTLINE: Randomized study for Radiation and Consolidation only. All patients enter Induction.

Induction.

Regimen A. 5-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; Vincristine, VCR, NSC-67574; VP-16213, VP-16, NSC-141540.

Radiation and Consolidation: Randomize partial responders (PR) and stable disease (SD) from Regimen A to Arms I and II; complete responders (CR) to Arms I and III. Patients with progressive disease from Regimen A go off study.

Arm I: Radiotherapy plus 2-Drug Combination Chemotherapy. High energy (not to exceed 6.0 MeV) whole brain irradiation and pre-induction field radiation technique, plus CTX and VP-16 sequentially.

Arm II: Radiotherapy plus 2-Drug Combination Chemotherapy. Post-induction field radiation technique, plus CTX and VP-16 sequentially.

Arm III: Radiotherapy plus 2-Drug Combination Chemotherapy. Whole brain irradiation as in Arm I, plus CTX and VP-16 concurrently.

Reinduction. Enter all patients upon completion of Radiation and Consolidation.

Regimen B. 5-Drug Combination Chemotherapy. ADR; CTX; MTX; VCR; VP-16. Upon completion of Reinduction, complete responders off treatment, patients with progressive disease off study. Patients with stable disease and partial responders receive 2-Drug Combination Chemotherapy. CTX; VP-16.

STRATIFICATION BY: Participating institutions, performance status, extent of tumor.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Duration of response, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 110-115 patients per year will be entered.

DOSAGE SCHEDULE:

Induction:

Regimen A (days 1 through 64): VCR - 2 mg iv on days 1, 8, 15, 22, 29, and 36; MTX - 60 mg/sqm iv on days 1 and 43; VP-16 - 50 mg/sqm/day iv infused in normal saline over 30-60 minutes on days 1 through 5 and 43 through 47; ADR - 60 mg/sqm iv on days 22 and 64; CTX - 1000 mg/sqm iv on days 22 and 64.

Radiation and Consolidation:

Arm I: 3000 rads in 10 fractions (5 days/week) on days 85 through 99 to whole brain. 1800 rads to chest (pre-induction technique) in 10 fractions on days 85 through 99, rest for 2 weeks, then 3000 rads in 12 fractions on days 114 through 130. Beginning on day 137, VP-16 - 120 mg/sqm iv infusion in normal saline over 30-60 minutes on days 1 and 8 q 4 weeks for 16 weeks; CTX - 750 mg/sqm iv on day 1 q 4 weeks for 16 weeks.

Arm II: 3000 rads to brain as in Arm I; 4800 rads to chest as in Arm I, except that field radiation is by the post-induction technique. CTX; VP-16 as in Arm I.

Arm III: 3000 rads to brain as in Arm I. VP-16; CTX as in Arm I, but given concurrently with radiation, and for 14 weeks thereafter.

Reinduction:

Regimen B: VCR; MTX; VP-16; ADR; CTX as in Regimen A. Upon completion, patients with complete response receive no further therapy but will be followed every 2 months during first year off therapy, every 3 months during second year and every 4-6 months thereafter. All patients will be followed until death. Patients with stable disease or partial response will receive VP-16 - 120 mg/sqm iv infusion on days 1 and 8 q 4 weeks, and CTX - 750 mg/sqm iv on day 1 q 4 weeks for indefinite period until there is evidence of progressive disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200, and 500 mg ampules; MTX - 50 mg vials; VCR - 1 and 5 mg ampules; VP-16 - 100 mg vials.

DATE SUMMARIZED: 02/80

7.0015 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE FOR REFRACTORY SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) SWOG-8009

OBJECTIVES:

I. Determine the response rate and remission duration in patients with refractory small cell lung cancer treated with dihydroxyanthracenedione on a single dose every-three-week schedule.

II. Define the qualitative and quantitative toxicities of dihydroxyanthracenedione in a Phase II study.

PROTOCOL ENTRY CRITERIA: Patients with pathologically verified histologic diagnosis of small cell lung cancer, with measurable disease, who are not eligible for studies with higher priority. The performance status must be 3 or better (SWOG criteria). The WBC count must be 3,500/cumm or greater and the platelet count 125, 000/cumm or greater. Patients must be past the nadir from previous therapy, particularly therapy with nitrosoureas or mitomycin-C. Serum creatinine and bilirubin must be 2.0 mg percent or less.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Fasting blood sugars; EKG; chest x-ray; tumor measurement scans or x-rays; hematologic, renal and hepatic function tests.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 14-25 patients will be entered.

DOSAGE SCHEDULE:

DHAD - 12 mg/sqm through a free-running iv over 30 minutes q 3 weeks. Patients who show disease progression after two courses go off study. Those who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 5 mg ampules.

DATE SUMMARIZED: 10/80

7.0016 INTENSIVE COMBINATION CHEMOTHERAPY WITH OR WITHOUT PROPHYLACTIC WHOLE BRAIN IRRADIATION FOR SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) BCRP-7705

OBJECTIVES:

I. Assess the efficacy of cyclophosphamide/adriamycin/VP-16213 vs. cyclophosphamide/adriamycin/VP-16213 alternating with CCNU/methotrexate/procarbazine/vincristine in patients with small cell carcinoma of the lung, measuring the response rate, the disease-free interval, and the duration of survival.

II. Determine whether cranial irradiation given after complete remission is attained can alter the CNS recurrence rate.

PROTOCOL ENTRY CRITERIA: Patients with histologic evidence of small cell anaplastic carcinoma of the bronchus who have not received prior chemotherapy or radiotherapy. Patients may have received corticosteroids previously.

PROTOCOL OUTLINE: Randomized study. Randomize all patients to Arm I or Arm II. Randomize all CR from Arms I and II to Arms III and IV.

Arm I: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; VP-16213, VP-16, NSC-141540.

Arm II: 3-Drug Combination Chemotherapy alternating with 4-Drug Combination Chemotherapy. CTX, ADR, VP-16; alternating with CCNU, NSC-79037; Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; Procarbazine, PCB, NSC-77213.

Arm III: Prophylactic Whole Brain Radiotherapy.

Arm IV: No further treatment.

STRATIFICATION BY: Brain metastases (present or absent at time of entry).

SPECIAL STUDY PARAMETERS: Chest x-rays, whole lung tomograms, hematologic parameters, liver function tests, kidney function tests, isotopic scanning as indicated clinically, CEA, BSP, systolic time intervals, fibroptic bronchoscopies.

END POINTS: Response/remission rate, duration of response, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CTX - 1000 mg/sqm iv on day 1; ADR - 45 mg/sqm iv on day 1 (total cumulative dose not to exceed 540 mg/sqm); VP-16 - 50 mg/sqm/day iv on days 1 through 5. Repeat cycles q 21 days.

Arm II: CTX/ADR/VP-16 as in Arm I for at least 3 courses and until patient achieves maximal tumor response, after which time alternate with 42-day courses of COMP: CCNU - 75 mg/sqm po on day 1; MTX - 40 mg/sqm iv on days 1 and 21; PCB - 75 mg/sqm/day po for 5 days beginning on days 1 and 21; VCR - 1.2 mg/sqm (maximum 2 mg) iv on days 1 and 21.

Treat all patients continuously until relapse with appropriate dosage modifications. All patients who fail on Arm I will be treated with CCNU/VCR/MTX/PCB as in Arm II. All patients with CR will be randomized to Arms III and IV.

Arm III: 3,000 rads cranial irradiation in 10 fractions of 300 rads each over 2 weeks. Patients who develop intracranial metastases after prophylactic irradiation will receive an additional 2400 rads in 300 rad fractions.

Arm IV: Observation only.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

7.0017 INTENSIVE COMBINATION CHEMOTHERAPY WITH ACE (ADR/CTX/VP-16) VS ACE-II (ADR/CTX/HD INFUSION VP-16) FOR SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) BCRP-8020

OBJECTIVES:

I. Determine whether increasing the dose of the single most active agent, VP-16123 (VP-16) given with adriamycin (ADR) and cyclophosphamide (CTX) and administering the VP-16 by continuous infusion can improve the response rate, the disease-free interval and the duration of survival in oat cell carcinoma.

II. Determine whether the addition of trimethoprim/sulfamethoxazole will effectively prevent severe infectious complications during periods of neutropenia brought on by the therapy.

PROTOCOL ENTRY CRITERIA: Patients with cytologic or histologic evidence of small cell (oat cell), anaplastic, undifferentiated carcinoma of the bronchus, measurable or nonmeasurable. Patients must not have had previous chemotherapy or radiotherapy but may have had corticosteroid treatment. Cranial metastases will receive whole brain irradiation. Single, isolated bone lesions may be present and will be biopsied if possible. There may be no other primary malignant disease except curatively treated basal cell carcinoma of the skin or of the cervix, in situ.

PROTOCOL OUTLINE: Randomized study. Initially randomize all patients to receive antibacterial agents or placebo. Rerandomize to Arm I or Arm II.

Arm I: 3-Drug Combination Chemotherapy. ACE: Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; VP-16213, VP-16, NSC-141540. ADR replaced by Methotrexate, MTX, NSC-740 upon maximum cumulative dose.

Arm II: 3-Drug Intensive Combination Chemotherapy. ACE-II: ADR; CTX; high-dose continuous infusion VP-16.

All patients who achieve complete remission will be given whole brain irradiation. Patients randomized to antibacterial agents receive Trimethoprim, NSC-106568, and Sulfamethoxazole.

STRATIFICATION BY: Disease stage.

SPECIAL STUDY PARAMETERS: Isotope scan of liver and bone, bilateral iliac crest bone marrow aspirations and biopsies, evaluation of paraneoplastic syndromes and paraendocrinopathies, EKG, MUGA scan, fiberoptic bronchoscopies.

END POINTS: Response/remission rate, recurrence rate, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: 130 patients will be entered.

DOSAGE SCHEDULE:

Arm I: ADR - 45 mg/sqm iv on day 1, maximum cumulative dose 540 mg/sqm, after which MTX - 40 mg/sqm iv will be given on day 1; CTX - 1000 mg/sqm iv on day 1; VP-16 - 50 mg/sqm/day iv one-hour infusion on days 1 through 5. Repeat q 21 days for 3 courses.

Arm II: ADR, CTX as in Arm I. VP-16 - 100 mg/sqm/day iv continuous infusion for 5 days. Repeat q 21 days for 3 courses.

During the first 3 courses, all patients initially randomized to antibacterial or placebo will receive either Trimethoprim, Sulfamethoxazole or placebo, double-blinded, 4 double-strength tablets/day in 2 divided doses (80 mg Trimethoprim, 320 mg Sulfamethoxazole).

All patients who are without brain metastases and who achieve complete remission will receive 3000 rads of whole brain irradiation in 10 fractions; those patients with brain metastases will receive 4800 rads; an additional 2400 rads in 8 fractions will be given to patients who develop cranial metastases subsequent to prophylactic irradiation. Upon completion of 3 courses, a 4-week rest period will follow, after which treatment will be renewed at a modified dose regimen for 2 years, or until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

7.0018 PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE (AZQ) FOR PREVIOUSLY TREATED SMALL CELL CARCINOMA

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PROTOCOL NUMBER(S) BCRP-8024

OBJECTIVES:

I. Determine response rate and remission duration in previously treated patients with advanced recurrent small cell carcinoma treated with aziridinylbenzoquinone used as a single dose given on days 1 and 8 on a 28-day cycle.

II. Define the qualitative and quantitative toxicities of AZQ administered in a Phase II study.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven small cell (oat cell) carcinoma with measurable disease who have failed conventional chemotherapy and who are not eligible for any other protocol of higher priority. Patients must have a minimum life expectancy of 6 weeks and a performance status better than 4. Adequate bone marrow, liver, and renal function is required. Patients must not receive chemotherapy or radiotherapy for the 4 weeks prior to entry (8 weeks for nitrosoureas) unless there is unequivocal evidence of rapid tumor progression.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Aziridinylbenzoquinone, AZQ, NSC-182986.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; tumor measurement; EKG; scans and/or x-rays.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: At least 14 patients will be required. If responses are observed, at least 25 patients will be entered.

DOSAGE SCHEDULE:

AZQ - 20 mg/sqm through a freely running iv over 15-30 min on days 1 and 8. Repeat treatment q 28 days. Retreatment may be delayed until the patient has recovered from drug-induced toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZQ - 10 mg vials.

DATE SUMMARIZED: 12/80

7.0019 CONTINUOUS VS ALTERNATING VOCAP (VCR/VP-16/CTX/ADR/CACP) VS VCP (CTX/CACP/VP-16) FOR EXTENSIVE SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) MAYO-782003

OBJECTIVES:

I. Evaluate and compare the continuous use of 5-drug regimens VOCAP-3 and VOCAP-1 (VCR/VP-16/CTX/ADR/CACP) with the alternating use of the same 5 drugs given in alternating 2- and 3-drug combinations VCP-3, VCP-1 (CTX/CACP/VP-16) and AO (ADR/VCR).

II. Compare the results obtained following 3 courses of VOCAP-3 vs. 3 courses of VCP-3 from the viewpoints of CR rates and toxicity.

III. Compare the results of 3 courses of VOCAP-1 (courses 4-6) with 3 courses of alternating AO and VCP-1 (courses 4-6) from the viewpoints of further tumor reduction and increasing the percentage of CR's.

IV. Compare the 2 regimens in their entirety from the viewpoints of regression rates, times to progression, and survival.

V. Determine if either program is potentially curative by discontinuing treatment after 10 courses in patients achieving CR status.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with cytologically and histologically proven measurable or evaluable small cell lung tumor with extensive disease or limited disease with an ECOG performance status of 3 or 4. Patients must have adequate hematological and cardiac functions, a normal serum creatinine, and a 5-year disease-free interval since any prior malignancy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Continuous 5-Drug Combination Chemotherapy. VOCAP-3: Vincristine, VCR, NSC-67574; VP-16, NSC-141540; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875; followed by VOCAP-1: VCR; VP-16; CTX; ADR; CACP, different dosages.

Arm II: 3-Drug Combination Chemotherapy followed by 3-Drug Combination Chemotherapy alternating with 2-Drug Combination Chemotherapy. VCP-3 and VCP-1: CTX; CACP; VP-16; alternating with AO: ADR; VCR.

Regimen A: Enter patients who do not achieve CR in Arm I or II. 2-Drug Combination Chemotherapy. VC: CTX; VP-16.

Radiation Therapy: Selectively enter only patients with extensive disease. Give standard palliative dose to one indicator lesion during the first 2 courses of Chemotherapy, or after 10 courses of Chemotherapy.

CNS Radiotherapy plus Hormone Therapy for patients with CNS metastases. Supervoltage: Cobalt-60 teletherapy or 4 MEV linear accelerator, plus oral Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Disease stage: extensive vs. limited with PS of 3 or 4; performance status: 0.2 vs. 3-4; age: less than 65 years old vs. more than 65 years old.

SPECIAL STUDY PARAMETERS: CAT scan; bone, brain, and liver scans; bone marrow biopsies; bone survey and liver biopsy if indicated.

END POINTS: Response/remission rate, objective tumor response, recurrence rate, toxicity/morbidity of treatment, survival rate.

CURRENT STATUS: 90-100 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: VOCAP-3 given q 4 weeks for 3 courses. Sequentially administer: CTX - 125 mg/sqm iv push on days 1, 2, and 3; ADR - 12.5 mg/sqm iv push on days 1, 2, and 3; VCR - 1.2 mg/sqm iv push on day 1 only; VP-16 - 75 mg/sqm iv 30 minute infusion on days 1, 2, and 3; CACP - 15 mg/sqm iv 60 minute infusions on days 1, 2, and 3. Remove nonresponders (NR) from study. Continue responders on VOCAP-1 for 7 courses given q 5 weeks for 3 courses and q 6 weeks thereafter. Sequentially administer on day 1: CTX - 375 mg/sqm iv; ADR - 37.5 mg/sqm iv; VCR - as in VOCAP-3; CACP - 40 mg/sqm; VP-16 - 225 mg/sqm iv 60 minute infusion plus 25 gm mannitol. Discontinue therapy for complete responders (CR). Enter patients with less than CR to Regimen A.

Arm II: VCP-3 given q 4 weeks for 3 courses. Sequentially administer on days 1, 2, and 3: CTX - 250 mg/sqm iv push; VP-16 - 75 mg/sqm iv push 40 minute infusion; CACP - 15 mg/sqm iv push 60 minute infusion. Remove NR from study. Continue CR with VCP-1 alternating with AO for 7 courses given q 5 weeks for 3 courses and q 6 weeks thereafter. VCP-1 given sequentially on day 1: CTX - 750 mg/sqm iv push; CACP - 40 mg/sqm iv push; VP-16 - 225 mg/sqm iv 60 minute infusion plus 25 gm mannitol; alternating with AO: ADR - 60 mg/sqm iv push on day 1; VCR - 62 mg/sqm iv push. Discontinue Chemotherapy for CR. Enter less than CR patients to Regimen A.

Regimen A: On day 1 give CTX - 750 mg/sqm iv push followed by VP-16 - 225 mg/sqm iv 60 minute infusion. Repeat course q 6 weeks.

Radiation Therapy: For CNS metastases: Irradiate whole brain - 2000 rad in 5 to 7 days, rest 3 weeks, 1600 rad in 5 to 7 days plus PRED - 60 mg/sqm given in 3 divided doses po 48 hours before and during each 5-day course, 30 mg po in 3 divided doses between courses, then taper to discontinue in 12 weeks after Radiotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; CACP - 10 mg vials; VCR - 1 and 5 mg vials; VP-16 - 100 mg ampules.

DATE SUMMARIZED: 04/79

7.0020 CHEMOTHERAPY WITH CTX, CCNU, VP-16, VCR, CACP, MTX, ADR AND VBL, AND/OR RADIOTHERAPY FOR HIGH AND LOW TUMOR BURDEN SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) MAYO-792001

OBJECTIVES:

I. Evaluate new drug regimens, all based on active predecessors, in patients with small cell lung cancer.

II. Compare the clinical efficacy of the present staging system vs. the system used in protocol MAYO-762001.

PROTOCOL ENTRY CRITERIA: Patients less than 75 years of age with histological or cytological diagnosis of small cell lung cancer, a performance status (PS) of 3 or 4, or with any PS and abnormal cardiac status, or with resected small cell lung cancer at any stage, with any cardiac or performance status. Patients must have adequate hematologic, liver and kidney function and must not have had prior thoracic radiation or chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study. Patients with high tumor burden (HTB) have one or more of the following: disease beyond ipsilateral supraclavicular fossae; evidence of metastases by chest x-ray; ECOG PS of 3 or 4; more than 5% weight loss in preceding 3 months; and/or anemia. Patients with low tumor burden (LTB) do not have the above symptoms. Enter HTB and LTB patients sequentially to Regimens A through D. Restage, then enter LTB to Regimen E or F. Enter HTB to Regimen G or H.

Regimen A: 5-Drug Combination Chemotherapy and Radiotherapy plus Hormone Therapy. CCVVP: Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037; VP-16213, VP-16, NSC-141540; Vincristine, VCR, NSC-67574; Cis-platinum, CACP, NSC-119875; plus CNS Radiation with Cobalt-60 Teletherapy or 4 MV linear accelerator; plus Prednisone, PRED, NSC-10023.

Regimen B: 4-Drug Combination Chemotherapy. CCVV: CTX; CCNU; VP-16; VCR.

Regimen C: 2-Drug Combination Chemotherapy plus Radiotherapy. CV: CTX; VP-16; plus thoracic Radiation with 4 or 10 MV linear accelerator.

Regimen D: 4-Drug Combination Chemotherapy. CCVV: CTX; CCNU; VP-16; VCR.

Regimen E: Enter LTB complete responders (CR). No further treatment.

Regimen F: Enter LTB patients with less than CR. 3-Drug Combination Chemotherapy alternating with 4-Drug Combination Chemotherapy. AVM: Adriamycin, NSC-123127; Vinblastine, VBL, NSC-49842; Methotrexate, MTX, NSC-740; alternating with CCVV.

Regimen G: Enter HTB with CR. 3-Drug Combination Chemotherapy. AVM.

Regimen H: Enter HTB with less than CR. 3-Drug Combination Chemotherapy alternating with 4-Drug Combination Chemotherapy. AVM and CCVV.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Bone and liver scans, brain CAT scan.

END POINTS: Response/remission rate, objective tumor response, survival.

CURRENT STATUS: 40 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Regimen A: CCVVP: CTX - 450 mg/sqm iv push on day 1; CCNU - 40 mg/sqm po on day 1; VP-16 - 75 mg/sqm iv in normal saline on days 1, 2 and 3; VCR - 1.2 mg/sqm iv push on day 3; CACP - 40 mg/sqm in dextrose saline with mannitol iv push on day 2. Repeat course in 4 to 5 weeks. Whole Brain Radiation - 1800 rads in 5 fractions over 5 to 7 days using lateral parallel opposed portals. Rest 3 weeks and repeat course with CCVVP chemotherapy. Give PRED - 60 mg/day po in 3 divided doses 2 days prior to and during CNS Radiation. Stop PRED during rest in patients without CNS metastases, if CNS metastases are present, give 40 mg/day in 4 divided doses in the first week, 30 mg/day in 3 divided doses in the second week and 20 mg/day in 2 divided doses in the third week. Taper PRED following second CNS Radiation treatment.

Regimen B: CCVV: CTX; CCNU; VP-16; VCR as in Regimen A for one course.

Regimen C: CV: CTX - 700 mg/sqm iv push on day 1; VP-16 - 70 mg/sqm iv push on days 1, 3, and 5. Give 2 courses. Give Thoracic Radiation to primary tumor, hilar and mediastinal lymph nodes and involved ipsilateral supraclavicular fossa - 2000 rads in 5 fractions over 5 to 7 days. Rest 3 weeks. Repeat course. Maximum dose to spinal cord is 3600 rads in 10 fractions over 5 weeks.

Regimen D: CCVV, as in Regimen B, for one course. Rest for 8 weeks, then restage patients and enter to appropriate subsequent therapy.

Regimen E: No further therapy.

Regimen F: AVM: ADR - 45 mg/sqm iv push on day 1; VLB - 4.5 mg/sqm iv push on day 1; MTX - 25 mg/sqm iv push on day 1 alternating with CCVV as in Regimen B for a total of 6 courses.

Regimen G: AVM, as in Regimen F, for 3 courses.

Regimen H: AVM, as in Regimen F, for a total of 6 courses.

Remove patients with progression from study during any Regimen.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; CCNU - 10, 40, and 100 mg capsules; ADR - 10 and 50 mg vials; VBL - 10 mg vials; MTX - 2 ml vials; VCR - 1 and 5 mg vials.

DATE SUMMARIZED: 12/79

7.0021 CHEMOTHERAPY WITH C2AV2 (CTX/CCNU/ADR/VP-16/VCR) FOLLOWED BY RADIOTHERAPY PLUS CHEMOTHERAPY FOR LIMITED SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) MAYO-792004

OBJECTIVES:

I. Determine effects of combination chemotherapy with C2AV2: cyclophosphamide (CTX)/CCNU/adriamycin (ADR)/VP-16213 (VP-16)/vincristine (VCR) followed by thoracic radiotherapy with CTX/VP-16 with and without ADR followed by whole brain radiotherapy with and without C2AV2 for limited, small cell undifferentiated lung cancer.

PROTOCOL ENTRY CRITERIA: Patients up to 70 years of age with histologically or cytologically confirmed, limited (confined to 1 hemithorax, ipsilateral hilum, ipsilateral and central mediastinum, and ipsilateral supraclavicular space), small cell, undifferentiated lung cancer with gross or microscopic/macroscopic residual tumor. Patients must have: ECOG performance status of at least 2, adequate kidney function, normal liver function, and serum sodium less than 120. Patients must not have: malignant pleural infusion, any prior pulmonary resection, or thoracic or CNS irradiation or chemotherapy.

PROTOCOL OUTLINE: Randomized study. Following treatment on Regimen A, patients are randomized to Arms IA and IB. Following treatment on Arm IA or IB patients are rerandomized to Arms IIA and IIB.

Regimen A: 5-Drug Combination Chemotherapy. C2AV2: Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037; Adriamycin, ADR, NSC-123127; VP-16213, VP-16, NSC-141540; Vincristine, VCR, NSC-67574.

Arm IA: 2-Drug Combination Chemotherapy. CTX; VP-16.

Arm IB: 3-Drug Combination Chemotherapy plus Radiotherapy. CTX; ADR; VP-16 plus 4 or 10 MeV linear accelerator irradiation of thorax.

Arm IIA: Radiotherapy plus 5-Drug Combination Chemotherapy. Cobalt-60 or 4 MeV linear accelerator irradiation of whole brain; C2AV2.

Arm IIB: Radiotherapy. Irradiation as in IIA.

STRATIFICATION: For Arm I: Response: complete remission vs. less than complete remission; sex: male vs. female; weight change since start of therapy: up vs. none vs. down. For Arm II: Response: complete remission vs. less than complete remission; chemotherapy in Arm I: CTX/VP-16 vs. CTX/ADR/VP-16; weight change: up vs. none vs. down.

SPECIAL STUDY PARAMETERS: Tumor measurement, PA, lateral and bilateral ducubitus chest x-ray, CTT brain scan, bone and liver scan, bone marrow aspirate and biopsy, bronchoscopy, 3-day sputum cytology.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 140 patients will be entered over 4 years.

DOSAGE SCHEDULE:

Regimen A: CTX - 450 mg/sqm iv push on day 3; CCNU - 40 mg/sqm po on day 1; ADR - 35 mg/sqm iv push on day 2; VP-16 - 50 mg/sqm iv push over 30 min on days 1, 2, and 3; VCR - 1 mg/sqm iv push on day 1 (give 1 mg on days 1, 8, and 15 in course #1); q 4 weeks for 3 courses.

Arm I: A. CTX - 125 mg/sqm iv push on days 1 through 5; VP-16 - 75 mg/sqm iv over 30 min on days 1, 3, and 5. B. CTX - 80 mg/sqm as in A; ADR - 40 mg/sqm iv push on day 1; VP-16 - as in A; 2000 rads in 5 fractions over 5 to 7 days for 2 courses (with 3-week rest between) to primary tumor, hilar and mediastinal lymph nodes, and involved ipsilateral supraclavicular fossa.

Arm II: 1800 rads in 5 fractions over 5-7 days for 2 courses with 3 week rest between to whole brain starting immediately for patients with CNS metastases and after 4 weeks for patients without CNS metastases; C2AV2 - as in Regimen A for 2 courses.

Remove from study patients in progression after any course of therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; CCNU - 10, 40, and 100 mg capsules; ADR - 10 and 50 mg vials; VCR - 1 and 5 mg vials; VP-16 - 100 mg ampules.

DATE SUMMARIZED: 02/80

7.0022 CHEMOTHERAPY WITH CCM PLUS ALTERNATING CCM/ADR/VCR VS CCM/ADR/VCR/VP-16 FOR EXTENSIVE SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) MAYO-792051; NCCTG-792051

OBJECTIVES:

I. Compare effect of combination chemotherapy with CCM: cyclophosphamide (CTX)/methotrexate (MTX)/CCNU followed by alternating CCM and adriamycin (ADR)/vincristine (VCR) vs. alternating CCM and ADR/VCR/VP-16213 (VP-16) for extensive small cell undifferentiated lung cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically-confirmed, measurable or evaluable, undifferentiated, small cell lung cancer with extensive metastases. Patients must have: adequate hematologic function, normal liver and kidney function, and ECOG performance status of at least 3. Patients must not have prior immunotherapy, radiotherapy, or chemotherapy for this tumor.

PROTOCOL OUTLINE: Randomized study. Randomize patients with stable disease or tumor regression after Regimen A to Arms I and II.

Regimen A: 3-Drug Combination Chemotherapy. CCM: Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037; Methotrexate, MTX, NSC-740.

Arm I: 5-Drug Alternating Combination Chemotherapy. CCM; alternating with Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574.

Arm II: 6-Drug Alternating Combination Chemotherapy. CCM; alternating with ADR; VCR; VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: ECOG performance status: 0 or 1 vs. 2 or 3; CNS: metastases vs. no metastases; age: up to 60 vs. over 60; response after Regimen A: complete remission vs. less than complete remission.

SPECIAL STUDY PARAMETERS: Tumor measurement; liver, kidney and bone function; liver, bone, and CNS scan; bone marrow aspirate and biopsy; bronchoscopy..

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 180 to 200 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Regimen A: CCM: CTX - 700 mg/sqm iv push on day 1; CCNU - 70 mg/sqm po on day 1; MTX - 20 mg/sqm on days 18 and 21; q 4 weeks for 2 courses.

Arm I: CCM: CTX - 500 mg/sqm iv push on day 1; CCNU - 50 mg/sqm po on day 1; MTX - 15 mg/sqm po on days 18 and 21. Alternate CCM q 3 weeks with ADR - 60 mg/sqm (maximum cumulative dose 480 mg/sqm) iv push on day 1; VCR - 1.2 mg/sqm (maximum dose 2 mg) iv push on day 1; q 3 weeks for 8 courses.

Arm II: CCM as in Arm I. Alternate CCM q 3 weeks with ADR - 40 mg/sqm iv push on day 1; VCR as in Arm I; VP-16 - 75 mg/sqm iv over 30 minutes on days 1, 2, and 3; q 3 weeks for 8 courses.

Give all patients CNS Radiotherapy - supervoltage irradiation of whole brain with 3000 rads in 10 fractions starting approximately day 88. Give immediate Radiotherapy to patients entering protocol with CNS metastases. If CNS metastases develop as only area of disease progression, irradiate and continue Chemotherapy. Give alternate Chemotherapy in same Arm to patients with first non-CNS progression. Remove from study patients with second non-CNS progression. Evaluate patients 6 weeks after the end of the 10 courses of therapy. If patient is in complete remission, discontinue treatment and recheck q 8 to 10 weeks for 18 months or until progression and removal from study. If patient is in less than complete remission without non-CNS progression during the 10 courses of therapy or with one non-CNS progression during ADR/VCR or ADR/VCR/VP-16 portions of the 10 courses of therapy, continue with CCM q 6 weeks and remove from study at first progression; with one non-CNS progression during CCM portion of the 10 courses of therapy, continue with ADR/VCR or ADR/VCR/VP-16 q 6 weeks and remove from study when total cumulative dose of ADR reaches 480 mg/sqm or progression occurs.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; VP-16 - 100 mg ampules, VCR - 1 and 5 mg vials; CCNU - 10, 40 and 100 mg capsules; MTX - 2.5 mg tablets.

DATE SUMMARIZED: 02/80

7.0023 MEGADOSE ECHO, BONE MARROW TRANSPLANTATION, BRAIN IRRADIATION, AND NUTRITIONAL THERAPY IN PEPA FOR SMALL CELL BRONCHOGENIC CARCINOMA

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PROTOCOL NUMBER(S) MDAR-329; MDA-DT-7914

OBJECTIVES:

I. Determine the efficacy of megadose combination chemotherapy with ECHO: VP-16213/cyclophosphamide/adriamycin/vincristine for limited disease small cell bronchogenic carcinoma.

II. Determine toxicity associated with this therapy.

III. Determine whether autologous bone marrow therapy (BMT) ameliorates megadose-induced myelosuppression and associated risks of infection and bleeding in a setting of protected environment and prophylactic antibiotics (PEPA).

IV. Determine whether intravenous hyperalimentation (IVH) and no feeding by mouth (NPO) causes a lower incidence of chemotherapy-induced gastrointestinal toxicities.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with histologically confirmed, measurable, untreated small cell bronchogenic carcinoma. Patients must have adequate hematologic cardiac, renal and hepatic functions.

PROTOCOL OUTLINE: Randomized study. Patients eligible for the protected environment are concurrently treated on Regimen A.

Regimen A: Preventive therapy plus Bone Marrow Therapy. Autologous bone marrow transplant plus protected environment and prophylactic antibiotics.

Arm I:

Induction: 4-Drug Combination Chemotherapy plus Nutritional Therapy. ECHO: VP-16213; VP-16, NSC-141540; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; plus IVH without oral feeding.

Maintenance: 4-Drug Combination Chemotherapy plus Radiotherapy. ECHO; plus whole brain irradiation.

Arm II:

Induction: 4-Drug Combination Chemotherapy plus Nutritional Therapy. Arm I, with oral feeding.

Maintenance: 4-Drug Combination Chemotherapy plus Radiotherapy. As in Arm I.

STRATIFICATION: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, length of survival, objective tumor response.

CURRENT STATUS: 60 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Bone marrow cells, irradiated with 2500 rads, are reinfused on day 5 after start of Chemotherapy.

Arm I:

Induction: ECHO: VP-16 - 200 mg/sqm given in 2 doses iv q 12 hours on days 1-3; CTX - 1.5 mg/sqm iv on days 1-3; ADR - 80 mg/sqm iv on day 1; VCR - 1.5 mg iv on days 1 and 3. Repeat course once after hematologic recovery; IVP-NPO for 1 week before and after commencement of chemotherapy.

Maintenance: ECHO: VP-16 - 50 mg/sqm iv on days 3, 4, and 5; CTX - 500 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 1; VCR - 1.5 mg iv on days 1 and 8; all given q 3 to 4 weeks for 4 courses; 3000 rads in 10 fractions to midplane of the skull.

Arm II:

Induction: ECHO, as in Arm I; IVH, as in Arm I, with oral feeding.

Maintenance: ECHO and radiotherapy as in Arm I. After 4 courses of maintenance discontinue chemotherapy; and give X-ray therapy to lung primary of patients in partial remission and to chest of patients in complete remission.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

7.0024 HIGH-DOSE COMBINATION CHEMOTHERAPY WITH VP-16/CTX/VCR PLUS AUTOLOGOUS BONE MARROW TRANSPLANT FOR LIMITED OAT CELL CARCINOMA

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PROTOCOL NUMBER(S) MDAR-329R; MDA-DT-7914R

OBJECTIVES:

I. Determine whether megadose combination chemotherapy with VP-16/cyclophosphamide/vincristine can produce higher and longer lasting CR, longer survival, and even cures in patients with limited oat cell carcinoma.

II. Evaluate the toxicities associated with the administration of this therapy.

III. Determine whether autologous bone marrow infusion may be used to ameliorate treatment-induced myelosuppression and associated risks of infection and hemorrhage in a setting of PE and prophylactic antibiotics.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with histologically proven small cell bronchogenic carcinoma who have limited disease. Bone marrow cellularity must be at least 30 percent, and platelets and granulocytes must be greater than 100,000 and 2000, respectively. Patients must have measurable lesions; there must be no history of myocardial disease or an abnormal EKG.

PROTOCOL OUTLINE: Nonrandomized study for Induction and Maintenance. Following Maintenance, randomize CR to Arm I or II and enter all PR to Arm I.

Regimen A: Induction.

3-Drug Combination Chemotherapy plus Homologous Bone Marrow Transplantation. VP-16213, VP-16, NSC-141540; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574.

Regimen B: Maintenance.

3-Drug Combination Chemotherapy plus Radiotherapy. Adriamycin, ADR, NSC-123127; CTX; VCR. Prophylactic whole brain x-irradiation.

Arm I: Radiotherapy. Chest irradiation.

Arm II: No further treatment.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: About 20-30 patients will be entered per year.

DOSAGE SCHEDULE:

Regimen A: Induction. VP-16 - 200 mg/sqm/day for 3 days iv; CTX - 1.5 g/sqm/day for 3 days iv; VCR - 1.5 mg/day on days 1 and 3 iv. BMT on day 5. A second course of therapy will be given when the patient demonstrates full hematologic recovery from the first.

Regimen B: Maintenance. ADR - 50 mg/sqm iv on day 1; VP-16 - 50 mg/sqm/day iv for 3 days; VCR - 1.5 mg iv on days 1 and 8. Four courses will be given. Concurrently with the first course, prophylactic whole brain irradiation will be given: 3000 rads total dose over a 2-week period at 5 fractions per week via opposing lateral fields, each fraction delivering a tumor dose of 300 rads to the midplane of the skull. Enter all PR to Arm I; randomize CR to Arms I and II.

Arm I: Chest irradiation.

Arm II: No further treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

7.0025 COMBINATION CHEMOTHERAPY WITH NM/PCB/MTX/CF FOR PREVIOUSLY TREATED PATIENTS WITH EXTENSIVE SMALL CELL ANAPLASTIC LUNG CANCER

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PROTOCOL NUMBER(S) MDAR-368; MDA-M2/gm34

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with nitrogen mustard/procarbazine/methotrexate/citrovorum factor in patients with extensive small cell anaplastic lung cancer.

II. Prolong the duration of response and remission in these patients.

PROTOCOL ENTRY CRITERIA: Previously treated patients with extensive small cell anaplastic lung cancer diagnosed by biopsy or cytology. Patients must be less than 71 years of age, have a performance status of 50 percent or better, and have adequate liver and renal function. Only patients not eligible for protocols of higher priority will be eligible. Prior chemotherapy must not have included any of the protocol drugs.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 4-Drug Combination Chemotherapy. Mechlorethamine, NM, NSC-762; Procarbazine, PCB, NSC-77213; Methotrexate, MTX, NSC-740; Leucovorin, CF, NSC-3590.

Maintenance: 2-Drug Combination Chemotherapy. NM; MTX.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters.

END POINTS: Response/remission rates, toxicity/morbidity of treatment, duration of response/remission.

CURRENT STATUS: Up to 30 patients will be entered.

DOSAGE SCHEDULE:

Induction: NM - 6 mg/sqm iv on days 1 and 2; PCB - 150 mg/sqm/day po for the first 10 days of cycles 1 and 3; MTX - 1500 mg/sqm iv on day 1; CF - 10 mg/sqm iv q 6 hours for 12 doses beginning on day 2 and continuing for 72 hours. Repeat q 21 days for a total of 4 cycles. Enter PR and CR to Maintenance.

Maintenance: MTX - 75 mg/sqm iv bolus q 21 days; NM - 7.5 mg/sqm iv bolus q 21 days. Continue treatment for 18 months in all patients who remain in CR or stable PR.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

7.0026 CHEMOTHERAPY BY CONTINUOUS INFUSION OF VP-16213 OR VM-26 FOR ADVANCED OAT-CELL LUNG CANCER IN ADULTS

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PROTOCOL NUMBER(S) MDAR-369; MDA-DT-7988

OBJECTIVES:

I. Compare the clinical efficacy in terms of response rate and survival of continuous five-day intravenous infusion of VP-16213 (VP-16) and that of VM-26.

II. Determine the qualitative and quantitative toxicities of these compounds when given as single agents in a 5-day continuous infusion schedule.

PROTOCOL ENTRY CRITERIA: Patients at least 15 years of age, with histologic proof of metastatic oat-cell lung cancer with measurable lesions, who have failed prior chemotherapy not using VP-16 or VM-26. Life expectancy must be at least 12 weeks. Patients must have been off all previous therapies for the 4 weeks prior to entry, must show no evidence of toxic effects. There must be adequate bone marrow, liver, and renal functions.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. VP-16213, VP-16, NSC-141540.

Arm II: Single-agent Chemotherapy. VM-26, VM-26, NSC-122819.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Minimum of 25 patients will be entered on each arm; additional patients will be entered if response rates on each arm exceed 20 percent, or statistical considerations justify it.

DOSAGE SCHEDULE:

Arm I: VP-16 - 50 mg/sqm/day for 5 days continuous iv infusion. Repeat at 3-week intervals for a period of 2 years or 1 year after achieving complete remission, whichever is shorter. Dosage may be increased or decreased periodically depending on lowest absolute granulocyte and lowest platelet count. Doses range from 40 to 70 mg/sqm.

Arm II: VM-26 - 40 mg/sqm/day for 5 days continuous iv infusion. Repeat every 3 weeks for 2 years or 1 year after achieving complete remission. Doses range from 30 to 60 mg/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

7.0027 PROPHYLACTIC ANTIBIOTICS IN PE DURING CONSOLIDATION WITH CTX/VP-16/MTX/CF AFTER INDUCTION WITH VCR/IPP/ADR FOR SMALL CELL BRONCHOGENIC CARCINOMA

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PROTOCOL NUMBER(S) MDAR-383; MDA-DT-8003

OBJECTIVES:

I. Determine whether 3 courses of intensive, early consolidation chemotherapy administered in the PE result in a higher CR rate in patients with extensive small cell bronchogenic carcinoma.

II. Determine whether this intensive consolidation chemotherapy produces longer lasting remission, longer survival, and even cures in these patients.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven extensive small cell bronchogenic carcinoma who are not known to have CNS disease and who are not bed-ridden or unable to care for themselves. Patients may not be over the age of 70 and may not have received more than 2 weeks of treatment with any of the study chemotherapeutic agents. Patients must have measurable disease. There must be no history of myocardial disease or abnormal EKG.

PROTOCOL OUTLINE: Randomized study, for Consolidation only.

Regimen A: Induction. 3-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Ifosfamide, IPP, NSC-109724; Adriamycin, ADR, NSC-123127.

Regimen B: Consolidation. Randomize patients to Arm I or Arm II.

Arm I: 4-Drug Combination Chemotherapy in PE. Cyclophosphamide, CTX, NSC-26271; VP-16213, VP-16, NSC-141540; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590. Therapy in protected environment.

Arm II: 4-Drug Combination Chemotherapy. CTX; VP-16; MTX; CF.

Regimen C: Prophylactic CNS Irradiation. Enter all patients from Regimen B.

Regimen D: Maintenance. 3-Drug Combination Chemotherapy alternating with 4-Drug Combination Chemotherapy. VCR/IPP/ADR; alternating with CTX/VP-16/MTX/CF.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival rate, length of survival.

CURRENT STATUS: About 30 patients per year will be eligible. After 3 years there should be 40 patients on each arm.

DOSAGE SCHEDULE:

Regimen A: VCR - 2 mg iv on days 1 and 8; IPP - 1 g/sqm/day iv on days 1 through 5; ADR - 60 mg/sqm on day 1.

Regimen B: Patients in Arm I are treated in the PE; those in Arm II are treated on an outpatient basis.

Arm I: CTX - 1.2 g/sqm iv on day 1; VP-16 - 120 mg/sqm/day on days 2 through 4; MTX - 1.5 g/sqm on day 8; CF - 15 mg q 6 hours for 8 doses on days 9 and 10 and days 16 and 17. Courses repeated after recovery from myelosuppression from previous course for a total of 3 courses. Systemic prophylactic antibiotics will be started as close as possible to the initiation of Chemotherapy.

Arm II: CTX - 1 g/sqm iv on day 1; VP-16 - 100 mg/sqm/day on days 2 through 4; MTX - 1.5 g/sqm on day 8; CF - 60 mg/day in 4 divided doses on days 9, 10, 16, and 17. Courses repeated at 4-week intervals for a total of 3 courses.

Regimen C: 3000 rads over 2 weeks in 10 fractions via opposing lateral fields including the entire middle cranial fossa. Each fraction will deliver a tumor dose of 300 rads to the midplane of the skull.

Regimen D: VCR - 2 mg/day on days 1 and 8; IPP - 0.8 g/sqm/day on days 1 through 5; ADR - 50 mg/sqm on day 1. Alternate with CTX - 0.8 g/sqm on day 1; VP-16 - 80 mg/sqm on days 2 and 4; MTX - 1 g/sqm on day 8; CF - 60 mg/day on days 9 and 10. Patients receive a total of 6 courses, alternating one course of VCR/IPP/ADR with one course of VP-16/CTX/MTX plus CF protection. Courses will be given at 2-month intervals.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/80

7.0028 PHASE II EVALUATION OF VINDESINE PLUS CIS-PLATINUM FOR REFRACTORY SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) MDAR-384; MDA-DT-8005

OBJECTIVES:

I. Determine the efficacy of vindesine administered by continuous iv infusion plus cis-platinum in patients with refractory small cell carcinoma of the lung.

II. Determine the qualitative and quantitative toxicities of this therapeutic regimen.

III. Determine the duration of response and the duration of survival of patients receiving this treatment.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic small cell lung cancer who have failed on prior combination chemotherapy that did not include the protocol agents. Patients must have measurable lesions and a life expectancy of at least 12 weeks. Patients must be off prior chemotherapy, radiotherapy, and immunotherapy for at least 4 weeks prior to entry and must have adequate bone marrow, renal, and hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 25 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 0.6 mg/sqm/day by continuous iv infusion for 5 days; CACP - 80 mg/sqm on day 5 iv. Courses are repeated at 3-week intervals for a period of 2 years or 1 year after CR, whichever is shorter. Dosages may be escalated to 0.7 and 100 mg/sqm, respectively, when granulocytes are greater than 2000 and platelets greater than 100,000. Similarly, dosages may be decreased to 0.5 and 70 mg/sqm when counts are less than 1000 and less than 75,000, respectively.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

7.0029 COMBINATION CHEMOTHERAPY WITH ADR, CTX, VCR, CACP, VP-16, CCNU, PCB PLUS RADIOTHERAPY WITH/WITHOUT THYMOSIN FOR SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) MSKCC-7891R

OBJECTIVES:

I. Increase the complete remission rate, the duration of remission, and the survival of patients with small cell carcinoma of the lung (SCCL).

II. Assess the effect (on remission rates and survival) of a putative immunopotentiator, thymosin (administered during the Induction phase of therapy), Induction chemotherapy with adriamycin/cyclophosphamide/vincristine plus cis-platinum/VP-16213, Consolidation with radiotherapy and cyclophosphamide/methotrexate/procarbazine, and Maintenance with CCNU/methotrexate/procarbazine and adriamycin/cyclophosphamide/vincristine and cis-platinum/VP-16213.

PROTOCOL ENTRY CRITERIA: Patients with histologically or cytologically proven small cell carcinoma of the lung. Patients must have a general medical condition suitable for aggressive systemic therapy, serum creatinine less than 1.4 mg percent, no history of malignant disease except for basal cell carcinoma of the skin, no evidence of congestive heart failure or recent history of angina pectoris, and no prior therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I:

Induction: Immunotherapy plus 3-Drug Combination Chemotherapy cycled with 2-Drug Combination Chemotherapy. Thymosin, no NSC; plus Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; plus cis-Platinum, CACP, NSC-119875; VP-16213, VP-16, NSC-141540.

Consolidation: Immunotherapy plus 2-Drug Combination Chemotherapy plus Radiotherapy. Thymosin plus CTX; VCR; plus Co-60 radiation. All responders go to Maintenance.

Maintenance: Two 3-Drug Combinations of Chemotherapy cycled with 2-Drug Combination Chemotherapy. CCNU, NSC-79037; Methotrexate, MTX, NSC-740; Procarbazine, PCB, NSC-77213; plus CTX; ADR; VCR; cycled with CACP; VP-16.

Arm II:

Induction: 3-Drug Combination Chemotherapy cycled with 2-Drug Combination Chemotherapy. CTX; ADR; VCR; plus CACP; VP-16 as in Arm I Induction.

Consolidation: 2-Drug Combination Chemotherapy plus Radiotherapy. CTX; VCR; plus Co-60 radiation as in Arm I Consolidation.

Maintenance: Two 3-Drug Combinations of Chemotherapy cycled with 2-Drug Combination Chemotherapy. CCNU; MTX; PCB; plus CTX; ADR; VCR; cycled with CACP; VP-16 as in Arm I Maintenance.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests; neurological examination with screening lumbar puncture and CT scans of head; CEA; beta-subunit HCG; calcitonin; LDH isoenzymes; bone scan; chest x-ray; immunologic evaluation to include: DNCB sensitization and challenge, intradermal skin tests with recall antigens, T-gamma and T-mu markers on lymphocytes, assays for natural killer cells, LIF, plaque-forming cells, response of isolated lymphs to mitogens and candida antigens, assay for thymic serum factor and alpha-2 HS glycoprotein.

END POINTS: Response/remission rate, duration of response, length of survival.

CURRENT STATUS: 80 patients will be entered over a 2-year period.

DOSAGE SCHEDULE:

Arm I:

Induction: Thymosin - 60 mg/sqm sc twice a week from the start of therapy through the conclusion of Consolidation. CTX - 1200 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; VCR - 1.2 mg/sqm iv on days 1 and 8. As soon as WBC and platelets recover, CACP - 60 mg/sqm iv with prehydration on day 1; VP-16 - 120 mg/sqm iv on days 4, 6, and 8. As soon as blood counts recover repeat cycle, alternating the 3-drug combination with the 2-drug combination for a total of 4 cycles. Patients with limited disease showing progression after initial 3-drug Chemotherapy begin Consolidation Radiotherapy as soon as progression is documented; those with systemic progression go off protocol.

Consolidation: Continue Thymosin; begin Consolidation Chemotherapy as soon as blood counts recover after Induction Chemotherapy. CTX - 500 mg/sqm iv on days 1 and 15; VCR - 1.4 mg/sqm iv on days 1 and 15; Co-60 (6 MeV) - 500 rads daily in two 250-rad fractions for 3 consecutive days, followed by 4 days rest, then 300 rads daily for 5 days. Patients with extensive disease showing response receive prophylactic cranial irradiation simultaneously with Chemotherapy. Radiation to the primary is not given routinely but is reserved for the treatment of troublesome local symptoms. Patients with extensive disease showing progression receive Radiotherapy to the primary complex only for symptomatic local progression. Patients showing progression after Radiotherapy go off protocol and are transferred to Phase II drug treatment. All responders go to Maintenance.

Maintenance: All patients showing PR and those with extensive disease showing CR after Radiotherapy begin Maintenance as soon as recovery from Consolidation therapy has occurred. Patients with limited disease showing CR rest for 10 weeks and then begin Maintenance Chemotherapy. CCNU - 80 mg/sqm po on day 1; MTX - 30 mg/sqm iv on days 1, 8, 15, and 22; PCB - 100 mg/sqm po on days 1 through 14. After 6 weeks, CTX - 1000 mg/sqm iv; ADR - 30 mg/sqm iv; VCR - 1.4 mg/sqm iv. After 4 weeks, CACP - 50 mg/sqm with prehydration; VP-16 - 120 mg/sqm iv on days 4, 6, and 8. After a 10-week rest, patients with limited disease still showing CR receive a second cycle of Chemotherapy. All others receive a second cycle with no 10-week rest period. Patients with limited disease showing CR after a second course stop therapy and are observed. Patients with PR continue therapy until relapse. Those with extensive disease showing CR stop therapy after an 18-month disease-free period.

Arm II:

Induction: CTX; ADR; VCR; followed by CACP; VP-16 as in Arm I.

Consolidation: CTX; VCR; plus Co-60 (6 MeV) irradiation as in Arm I.

Maintenance: CCNU; MTX; PCB; followed by CTX; ADR; VCR; followed by CACP; VP-16 as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

7.0030 PILOT COMBINATION CHEMOTHERAPY WITH ADR/BCNU/VP-16 PLUS IMMUNOTHERAPY FOR SMALL CELL LUNG CARCINOMA IN FIRST RELAPSE

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PROTOCOL NUMBER(S) MSKCC-8024

OBJECTIVES:

I. Determine the nonhematologic toxicities of a combination of high doses of BCNU, VP-16213 (VP-16), adriamycin (ADR) and cyclophosphamide (CTX).

II. Verify that the cryopreservation techniques for autologous stem cell transplantation will insure hemopoietic reconstitution after presumed marrow ablation by high doses of chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with small cell carcinoma of the lung who have relapsed after primary therapy and at the time of relapse show no evidence of bone marrow involvement will be entered for marrow procurement. Patients who have attained complete remission after prior treatment but have a high likelihood of relapse may be entered for marrow procurement and cryopreservation for treatment at the time of first relapse. The performance status must be 60 or better (Karnofsky) and the disease must be measurable at the time of relapse. The general medical condition must be sufficient to allow for general anesthesia. There must be no clinical or laboratory evidence of cardiomyopathy, and the serum bilirubin must be less than 2.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy plus Immunotherapy. BCNU, NSC-409962; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; VP-16213, VP-16, NSC-141540; plus Autologous Bone Marrow Therapy.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Gated blood pool scan; liver function; liver, spleen, brain and CTT scans; pulmonary function.

END POINTS: Response/remission rate, disease-free interval, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 15 patients will be entered.

DOSAGE SCHEDULE:

BCNU - 300 mg/sqm on days 1, 2 and 3; CTX - 2400 mg/sqm on days 4 and 5; ADR - 60 mg/sqm on days 4 and 5; VP-16 - 120 mg/sqm on days 1 through 5; bone marrow on day 8. If there is complete or partial remission following one course of treatment, no further therapy is given until relapse or progression. If there is no response or disease progression following one course, additional Chemotherapy can be given when the WBC is 3000 or greater and platelet count is 150,000 or greater.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

7.0031 PHASE I-II HEMIBODY RADIOTHERAPY FOR PROGRESSIVE SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) NCI-77-C-171; NCI-MOB-772

OBJECTIVES:

I. Determine the toxic effects of hemibody radiotherapy in patients with small cell carcinoma of the lung who have failed intensive primary treatment with cytotoxic chemotherapy.

II. Determine the palliative and objective antitumor effects of hemibody radiotherapy in these patients.

III. Investigate various fractionation schemes in delivery of hemibody radiotherapy in order to find one that would be appropriate for combining with chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with histologically confirmed small cell carcinoma of the lung whose tumor has progressed on initial or later treatment programs. Patients must have evidence of extensive disease prior to or at the time of entry into the study; they must have no immediate need for localized chest radiotherapy for the relief of symptoms. Patients must not have received prior conventional chest radiotherapy. The patient must have adequate marrow function and an ECOG performance status of better than 4.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. 6 MeV linear accelerator or higher energy equipment.

STRATIFICATION BY: Site of maximum tumor load (upper half of body vs. lower half of body).

SPECIAL STUDY PARAMETERS: Hemogram, blood chemistries, chest x-ray, bone marrow biopsy, fiberoptic bronchoscopy, appropriate x-rays to measure tumor.

END POINTS: Objective tumor response, duration of response, toxicity/morbidity of treatment, response/remission rate, survival.

CURRENT STATUS: At least 14 patients will be entered.

DOSAGE SCHEDULE:

400 rads midplane dose/week to upper or lower half of the body depending on location of major tumor load. Repeat weekly to a maximum dose of 2000 rads. Discontinue treatment if objective progression of tumor occurs within the treatment area after 3 or more fractions have been delivered. If objective progression occurs outside the treatment field, the other half of the body will be treated, if the hematologic status permits. Follow patients until progression of disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 08/80

7.0032 PILOT COMBINATION CHEMOTHERAPY, RADIOTHERAPY AND IMMUNOTHERAPY FOR EXTENSIVE SMALL CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) NCI-80-C-67; NCI-VA-MOB-803

OBJECTIVES:

I. Increase the complete response rate and prolong the survival of patients with extensive stage small cell carcinoma of the lung.

II. Increase the duration of complete response and survival with intensive combined modality therapy in patients with extensive small cell carcinoma who enter complete response during 12 weeks of standard chemotherapy.

III. Convert patients with partial response after 12 weeks of combination chemotherapy to complete response status, by means of more intensive doses of one drug to which the patients have previously been exposed, one new drug, autologous hematopoietic reconstitution, and local irradiation to multiple areas initially involved with disease.

IV. Determine the frequency with which new complete responses are achieved with the present combined modality program, and document duration of complete response and survival in treated patients.

V. Document the toxicities, sites of response, and sites of disease progression when this late intensive combined modality program is employed.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed diagnosis of small cell carcinoma with a primary pulmonary lesion. In most cases, the disease must be judged inoperable and extensive. Patients must be 65 years old or younger (66-70 years with PS 0-2 if approved) and they must be at least partially ambulatory (PS 0-3). Patients must have received no prior radiotherapy or chemotherapy. Hematologic and renal functions must be adequate, and there may not be active infections, symptomatic heart disease, psychiatric problem or second malignancy. Intracranial or epidural metastases or impending pathologic bone fracture are acceptable if patient is otherwise eligible. Patient must be willing to receive blood product transfusions.

PROTOCOL OUTLINE: Nonrandomized study. All patients enter Regimen A. Those in PR with persistent disease in bone marrow following Regimen A therapy enter Regimen B; those in CR or PR with negative bone marrow enter Regimen C.

Regimen A: Induction. Sequential 3-Drug Combination Chemotherapy. CMC: Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037; Methotrexate, MTX, NSC-740; followed by VAP: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Procarbazine, PCB, NSC-77213.

Regimen B: Maintenance. Alternating 3-Drug Combination Chemotherapy. CMC alternating with VAP.

Regimen C: 2-Drug Combination Chemotherapy plus Radiotherapy plus Immunotherapy. CTX; VP-16213, VP-16, NSC-141540 plus Autologous Bone Marrow Therapy.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Fiberoptic bronchoscopy; bilateral iliac crest bone marrow aspirates and biopsies; radionuclide liver, brain and bone scans; CAT brain scan; liver biopsy; bone x-rays; nodal or subcutaneous masses aspirate or biopsy; tumor clonogenic assays; ECG; urine and blood analyses; skin tests; immunoelectrophoresis; lumbar puncture.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, length of survival, objective tumor response.

CURRENT STATUS: 30 patients will be entered in 18 months to 2 years.

DOSAGE SCHEDULE:

Regimen A: Induction: (Weeks 1-6) CMC: CTX - 1500 mg/sqm iv on days 1 and 22; CCNU - 100 mg/sqm po on day 1; MTX - 15 mg/sqm po on days 1, 4, 8, 11 and 22, 25, 29, 32. (Weeks 7-12) VAP: VCR - 1.4 mg/sqm iv (maximum dose 2 mg) on days 1 and 22; ADR - 60 mg/sqm iv on days 1 and 22; PCB - 100 mg/sqm po on days 1 through 10 and 22 through 31. (Week 13) Patients are completely restaged. Nonresponders go off study for individualized treatment. Complete and partial responders ineligible for late intensive combined modality therapy go to Regimen B for Maintenance; eligible patients go to Regimen C.

Regimen B: Maintenance: (Weeks 1-6) CMC: CTX - 500 mg/sqm iv on days 1 and 22; CCNU - 50 mg/sqm po on day 1; MTX - 10 mg/sqm po on days 1, 4, 8, 11 and 22, 25, 29, 32. (Weeks 7-12) VAP: VCR, ADR, and PCB as in Regimen A. Alternating 6-week cycles will continue until week 49, at which time patients will be completely restaged. Patients with complete response go off treatment; partial responders continue treatment. Patients with progressive disease go off study.

Regimen C: Autologous bone marrow is collected and placed in cryostorage (Week 14). Multiple field local irradiation - 2000 rads in 5 fractions over 5 days. If liver is involved with tumor, 1500 rads in fractions will be delivered over 5 days. Brain metastases receive 2000 rads in 5 fractions over 5 days (Week 15). On week 16, intensive Chemotherapy and autologous marrow infusion will begin, VP-16 - 200 mg/sqm iv daily for 3 days; CTX - 60 mg/sqm iv on days 2 and 3; autologous marrow infusion on day 5. During weeks 17 through 19, patients receive supportive care; they are restaged during week 20. Partial responders receive Maintenance therapy as given in Regimen B; complete responders go off treatment (Week 21). Prophylactic cranial irradiation, 2400 rads in 8 fractions over 2 weeks, will be given to patients without CNS metastases (Weeks 24 and 25). On week 49, complete responders go off treatment, partial responders continue therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

7.0033 CHEMOTHERAPY WITH VAV (VP-16/ADR/VCR) AND CCM (CTX/CCNU/MTX), RADIOTHERAPY, AND LEV IMMUNOTHERAPY FOR OAT-CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) WPL-7621; MDAR-125; RPMI-7621

OBJECTIVES:

I. Compare the therapeutic efficacy of a drug regimen consisting of VAV (VP-16213, adriamycin, and vincristine) to previous responses to other regimens including CCM (cyclophosphamide, CCNU, and methotrexate) for small cell undifferentiated, oat cell carcinoma of the lung.

II. Compare the effectiveness of alternating combinations of VAV and CCM with previous responses obtained with repetitive courses of CCM alone in this disease.

III. Determine the effectiveness of levamisole as an immunostimulant and as a therapeutic agent for oat cell lung carcinoma.

PROTOCOL ENTRY CRITERIA: Patients who have small cell undifferentiated carcinoma of the lung (oat cell carcinoma as defined by the Working Party for the Therapy of Lung Cancer) with both regional and extensive disease who have neither received radiotherapy to the primary site nor chemotherapy with the drugs of this protocol. Patients must have a minimum performance status of 3 and must have evaluable or measurable disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Radiotherapy followed by 3-Drug Combination Chemotherapy. VAV: VP-16, NSC-141546; Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; followed by CCM: Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037; Methotrexate, MTX, NSC-740.

Arm II: 3-Drug Combination Chemotherapy plus Radiotherapy plus Immunotherapy. VAV; CCM plus Radiotherapy, as in Arm I; plus Levamisole, LEV, NSC-177023.

STRATIFICATION BY: Performance status; disease status as measurable, evaluable, previously treated and regional or extensive.

SPECIAL STUDY PARAMETERS: SGOT, serum bilirubin, BUN, creatinine, creatinine clearance, Hb, alkaline phosphatase, PA and lateral chest films, DTH tests; optional - isotope bone scan and survey, uric acid, serum proteins and serum protein electrophoresis, calcium, phosphorus, isotope bone scan or survey.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, incidence of tumors, benefit to the patients as measured by performance status.

CURRENT STATUS: 128 patients will be entered.

DOSAGE SCHEDULE:

Arm I: VAV: VP-16 - 75 mg/sqm iv on days 1, 3 and 5 q 21 days; VCR - 1.5 mg/sqm (maximum 2.0 mg) on days 1 and 5; ADR - 45 mg/sqm single dose iv on day 5 and q 21 days. Radiotherapy total dose of 3000 rads, beginning on day 22. Repeat course of VAV once, then give one course of CCM: CTX - 600 mg/sqm single dose iv on day 1 and q 21 days; CCNU - 50 mg/sqm single dose po day 1 and q 6 weeks; MTX - 30 mg/sqm intramuscular on days 1 and 8 and q 21 days. Repeat VAV, giving 2 courses in 6 weeks. Patients go off study if disease progresses.

Arm II: Chemotherapy with VAV, CCM and Radiotherapy, as in Arm I, plus LEV - 100 mg/sqm po on days 8, 9, 15 and 16 during VAV and on days 10, 11, 17 and 18 during CCM.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VP-16 - 100 mg vials; ADR - 10 mg ampules; VCR - 1 and 5 mg ampules; CTX - 100, 200 and 500 mg vials; CCNU - 10, 40 and 100 mg capsules; MTX - 2.5 mg tablets and 50 mg vials; LEV - not given.

DATE SUMMARIZED: 03/77

7.0034 VOCA (VP-16/VCR/CTX/ADR) VS OCA (VCR/CTX/ADR) PLUS RADIOTHERAPY FOR LIMITED STAGE SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) NCCTG-792052

OBJECTIVES:

I. Compare the clinical effectiveness and adaptability of 2 chemotherapies: VOCA - VP-16/vincristine (VCR)/cyclophosphamide (CTX)/adriamycin (ADR) vs. OCA - VCR/CTX/ADR in a clinical oncology practice setting outside a major cancer research center.

II. Compare the toxicities of these regimens.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed small cell undifferentiated lung cancer limited to one hemithorax, the mediastinum, and ipsilateral supraclavicular fossa who have had no prior therapy of any kind. Patients must have adequate hematologic function, serum creatinine over 50% of upper limits of institutional norm, ECOG performance status of at least 3, and cardiac-pulmonary function adequate to permit thoracic irradiation.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Radiotherapy. OCA: Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127 plus supervoltage (Cobalt or linear accelerator) to thorax and prophylactic radiotherapy to CNS.

Arm II: 4-Drug Combination Chemotherapy plus Radiotherapy. VOCA: VP-16213, VP-16, NSC-141540; VCR; CTX; ADR; plus Radiotherapy as in Arm I.

Regimen A: For patients with non-CNS progression following 6 courses of protocol Chemotherapy. 3-Drug Combination Chemotherapy. CMP: CCNU, NSC-79037; Methotrexate, MTX, NSC-740; Procarbazine, PCB, NSC-77213.

STRATIFICATION: Participating institutions; performance status: 0 to 1 vs. 2 to 3; age: under 60 vs. over 60; sex; history of heart disease.

SPECIAL STUDY PARAMETERS: Liver and bone scan, bone marrow aspirate and biopsy, bronchoscopy, CTT or radionuclide brain scan, sputum cytology.

END POINTS: Response remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 150 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: OCA: VCR - 1.2 mg/sqm (maximum dose 2 mg); CTX - 750 mg/sqm (increase to 1000 mg/sqm when ADR is omitted; ADR - 40 mg/sqm (maximum total dose 450 mg/sqm), all given iv over 5 to 10 min on day 1 q 21 days for 3 courses, then q 28 days for 3 courses; 3900 rads in 13 fractions over 17 to 19 days to primary tumor, hilar and mediastinal lymph nodes, and involved supraclavicular fossa; 3000 rads in 10 fractions over 12 to 14 days to CNS including whole brain. Begin all radiotherapy in conjunction with the 4th course of chemotherapy omitting ADR dose for that course only.

Arm II: VOCA: VP-16 - 60 mg/sqm (increase to 75 mg/sqm when ADR is omitted) iv given in 30 min on days 1, 2, 3; VCR - as in Arm I; CTX -500 mg/sqm (increase to 650 mg/sqm when ADR is omitted) iv in 5 to 10 min on day 1; ADR - as in Arm I. Repeat course q 21 days for 3 courses, then q 28 days for 3 courses. Radiotherapy - as in Arm I.

Permanently discontinue ADR at first sign of new or worsening heart disease. During the 6 courses of Chemotherapy, remove from study patients in non-CNS or CNS progression following CNS Radiotherapy, and irradiate CNS and continue Chemotherapy for patients with CNS progression who have not had CNS irradiation. Eight weeks after completion of 6 courses of chemotherapy: stop therapy for patients in complete remission and follow up q 2 months for 1 year, then q 3 months for 1 year, then q 6 months; remove from study patients in CNS or other progression.

Regimen A: Enter patients in non-CNS progression after completion of 6 courses of Chemotherapy. CMP: CCNU - 50 mg/sqm po on day 1; MTX -10 mg/sqm po 2 times/week for 5 weeks; PCB - 100 mg/sqm po on days 1 through 10 and 22 through 31. Repeat course q 6 weeks until disease progression. Continue OCA and VOCA for patients in partial remission or stable disease until they achieve complete remission or disease progresses. For complete responders, give 2 more courses of Chemotherapy and follow up as above; and treat patients in CNS and non-CNS progression as above.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; ADR - 10 and 50 mg vials; VCR - 1.0 and 5.0 mg vials; VP-16 - 100 mg ampules; CCNU - 10, 40 and 100 mg capsules; MTX - 2.5 mg tablets; PCB - 50 mg capsules.

DATE SUMMARIZED: 11/79

7.0035 PHASE III CHEMOTHERAPY WITH CTX/ADR/VCR PLUS VP-16/MTX/CF WITH/WITHOUT TOTAL PARENTERAL NUTRITION FOR SMALL CELL ANAPLASTIC LUNG CARCINOMA

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PROTOCOL NUMBER(S) NUTR-7901

OBJECTIVES:

I. Determine the effect of total parenteral nutrition in patients with small cell anaplastic lung cancer as an adjunct to chemotherapy with CAV: cyclophosphamide (CTX)/adriamycin (ADR)/vincristine (VCR) and VMC: VP-16213 (VP-16)/methotrexate (MTX)/citrovorum factor (CF) plus Radiotherapy.

II. Determine tolerance to induction, response frequency and duration, survival duration, proportion of long term survivors, nutritional status and the effect of total parenteral nutrition on tumor growth.

PROTOCOL ENTRY CRITERIA: Patients with evaluable, histologically or cytologically proven small cell anaplastic carcinoma of the lung. Patients must have adequate bone marrow, hepatic and renal function, an ECOG performance status of 3 or less and a minimum life expectancy of 8 weeks. Patients must have no prior chemo- or radiotherapy, have adequate cardiac status, be 75 years old or less and be free of CNS metastases.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arm I or Arm II. Enter nonresponders to Arm III. Enter responders to Arm IV.

Arm I: 3-Drug Combination Chemotherapy. CAV: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574.

Arm II: 3-Drug Combination Chemotherapy plus Total Parenteral Nutrition. CAV: CTX/ADR/VCR.

Arm III: 3-Drug Combination Chemotherapy: VMC: VP-16213, VP-16, NSC-141540; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

Arm IV: 3-Drug Combination Chemotherapy. VMC; followed by CAV in modified dosage.

STRATIFICATION BY: Participating institutions; ECOG performance status: 0, 1 vs. 2 vs. 3; disease extent: limited vs. extensive; weight loss: less than 2 percent of normal weight vs. more than 2 percent.

SPECIAL STUDY PARAMETERS: Liver-spleen, bone, and brain scans; skin test immunology; delayed hypersensitivity.

END POINTS: Objective tumor response, response/remission rate, survival time, duration of response.

CURRENT STATUS: At least 270 patients to be entered.

DOSAGE SCHEDULE:

Arm I: CAV: CTX - 1200 mg/sqm iv on day 1; ADR - 70 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on day 1; VCR - 2 mg iv on day 1. Repeat q 3 weeks for 2 courses.

Arm II: CAV as in Arm I, plus total parenteral nutrition.

Arm III: VMC: VP-16 - 100 mg/sqm iv on days 1 through 3; MTX - 50 mg/sqm iv on day 1; CF - 30 mg/sqm po or iv in 6 divided doses every 6 hours beginning 36 hours after MTX; repeated q 3 weeks until progression. Responders receive prophylactic Radiotherapy after the second VMC course.

Arm IV: Modified CAV: VCR as in Arm I; CTX - 1000 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; repeated q 3 weeks for 2 courses. Patients responding after 2 courses receive prophylactic Radiotherapy. Modified CAV is followed by VMC as in Arm III for 5 courses or until progression, modified CAV until maximum dose of ADR or progression, and VMC for 5 courses or until progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

7.0036 ADR/MTX/CTX/CCNU CHEMOTHERAPY PLUS C. PARVUM IMMUNOTHERAPY WITH AND WITHOUT DEHYDROEMETINE/VCR/BLEO FOR SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) EORTC-08764

OBJECTIVES:

I. Determine if the addition of Dehydroemetine, Vincristine (VCR) and Bleomycin (BLEO) to an immunochemotherapeutic regimen of Adriamycin (ADR), Methotrexate (MTX), Cyclophosphamide (CTX), CCNU, and C. parvum modifies the response rate and the duration of response.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with small cell lung cancer confirmed by biopsy or exploratory surgery. Patients must have an evaluable lesion, a performance status of 3 or less, no prior radiotherapy, chemotherapy nor excision surgery. Patients must have an adequate white cell and platelet count and no cerebral metastases or coronary occlusion within the past 6 months.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy plus Immunotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; CCNU, NSC-79037; plus C. parvum Merieux, C. parvum, NSC-197213.

Arm II: 4-Drug Combination Chemotherapy plus Immunotherapy followed by 3-Drug Combination Chemotherapy. ADR, CTX, MTX, CCNU, C. parvum plus Bleomycin, BLEO, NSC-125066; Vincristine, VCR, NSC-67574; Dehydroemetine, NSC-131546.

STRATIFICATION BY: Tumor site: localized lesion in the thorax vs. disseminated lesion outside of thorax (liver, bone, extrathoracic ganglion, skin).

SPECIAL STUDY PARAMETERS: Bone scan, bone marrow biopsy, fiberoptic bronchoscopy.

END POINTS: Response/remission rate, duration of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: ADR - 60 mg/sqm (maximum cumulative dose 500 mg/sqm); CTX -800 mg/sqm; MTX - 40 mg/sqm. Give all 3 drugs iv in 125 ml normal serum; plus CCNU - 60 mg/sqm po on the same day; plus C. parvum - 4 mg im q week. Repeat course q 4 weeks for a minimum of 12 weeks.

Arm II: Chemoimmunotherapy, as in Arm I; plus BLEO - 15 mg (maximum cumulative dose 300 mg) im; VCR - 1 mg iv; Dehydroemetine - 120 mg im; all 3 given once a week for 3 weeks, when Arm I therapy is not given, for a minimum of 12 weeks.

Continue partial responders, complete responders or patients with no change on therapy as long as it appears to be effective. Remove from study patients with disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 20, 25 and 50 mg ampules; CTX - 100 and 500 mg ampules; ADR - 10 and 50 mg ampules; CCNU - 40 mg capsules; VCR - 1 mg ampules; BLEO - 15 mg ampules; Dehydroemetine - 60 mg ampules; C. parvum - 4 mg ampules.

DATE SUMMARIZED: 07/79

7.0037 COMBINATION CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE/METHOTREXATE/CCNU WITH VS WITHOUT VP-16213 FOR OAT CELL LUNG CANCER

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PROTOCOL NUMBER(S) ITA-MIL-LC793

OBJECTIVES:

I. Compare the efficacy of and adverse reactions to a chemotherapeutic schedule with cyclophosphamide (CTX)/Methotrexate (MTX)/CCNU/VP-16213 (VP-16) vs. CTX/MTX/CCNU in oat cell lung cancer.

II. Assess the effect of VP-16 on the primary tumor.

III. Assess the effect of VP-16 in the prevention of cerebral metastases.

IV. Compare the utility of a modified CTX/MTX/CCNU schedule with findings described for the original schedule in the literature.

PROTOCOL ENTRY CRITERIA: Patients under 71 years old with residual oat cell bronchogenic carcinoma diagnosed by bronchial, nodal or metastatic biopsy. Patients must have a performance status of at least 40, and must not have had prior radiation or chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Induction, Consolidation and Maintenance. 4-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; CCNU, NSC-79037; VP-16213, VP-16, NSC-141540.

Arm II: Induction, Consolidation and Maintenance. 3-Drug Combination Chemotherapy. CTX; MTX; CCNU.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Bronchoscopy, immunological status.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of response, survival, quality of life.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Induction. CTX-1000 mg/sqm iv on day 1; VP-16 - 500 mg/sqm iv divided over days 1 to 3, repeat CTX, VP-16 q 21 days for 3 courses; MTX-25 mg/sqm iv on day 1 q 7 days; CCNU - 80 mg/sqm po on day 1, repeat CCNU in 6 weeks. Evaluate all patients in 8 or 9 weeks.

Consolidation: Enter all patients with complete or partial response 4 weeks after their last 21-day course; remove all other patients from study. CTX, VP-16 as in Induction; MTX - 25 mg/sqm iv on day 1; CCNU - 40 mg/sqm po on day 1. Repeat course q 28 days for 3 courses, then re-evaluate all patients.

Maintenance: Enter all patients with complete or partial response 8 weeks after last course of therapy. Remove all other patients from study. CTX, VP-16, MTX, CCNU as in Consolidation. Repeat course q 2 months for at least 6 months or until disease progression.

Arm II: Induction. CTX, MTX, CCNU as in Arm I Induction.

Consolidation: Enter patients with complete or partial response after 4 weeks after their last course, remove all other patients from study. CTX, MTX, CCNU, as in Arm I Consolidation.

Maintenance: Enter all patients with complete or partial response 8 weeks after their last course, remove all other patients from study. CTX, MTX, CCNU, as in Arm I Maintenance.

Remove from study patients with stable disease for 3 months, progressive disease, hematologic or refractory gastroenteric toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

7B. LUNG TUMORS—GENERAL

7.0038 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED NON-SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) CLB-8071

OBJECTIVES:

I. Determine the complete and partial response frequency, duration of response and survival of patients with measurable or evaluable locally advanced and/or metastatic non-small cell anaplastic lung carcinoma treated with methyl-GAG (MeGAG).

II. Determine the toxicity of MeGAG.

PROTOCOL ENTRY CRITERIA: Patients with measurable or evaluable, histologically proven locally advanced and/or metastatic non-small cell carcinoma of the lung. Tumor types include: squamous cell carcinoma; adenocarcinoma, including bronchioalveolar carcinoma (and those formerly classified as large cell anaplastic carcinoma with mucin production, Addendum 1, April 1980); and large cell anaplastic carcinoma, including giant cell and clear cell. Patients must be at least 16 years of age and must have a CALGB performance status of 2 or less and adequate hematologic status. (BUN must be no more than 25 mg/dl, and creatinine no more than 1.5 mg/dl. Patients with liver function abnormalities and those with large pleural effusions, ascites, or edema are eligible. Addendum 1, April 1980.) Patients must have no prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

STRATIFICATION BY: Participating institutions; measurable vs. evaluable disease; disease type: squamous cell carcinoma vs. adenocarcinoma and large cell carcinoma.

SPECIAL STUDY PARAMETERS: Liver and bone scan, skin testing for delayed hypersensitivity.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 70 to 100 patients to be entered in 6 to 9 months.

DOSAGE SCHEDULE:

MeGAG - 500 mg/sqm iv weekly, escalating to 600 mg/sqm in 50 mg/sqm steps q 3 weeks if toxicity permits. (Addendum 1, April 1980. Initial dose modified to 650 mg/sqm weekly for 3 weeks, then increasing, toxicity permitting, to 700 mg/sqm for 3 weeks, then increasing by 50 mg/sqm q 3 weeks. Patients with large pleural effusions, ascites, or edema begin at 500 mg/sqm, increasing, after 3 weeks, by 50 mg/sqm q 3 weeks until dose-limiting toxicity.) (Addendum 2, October 1980. Dosages are increased by 50 mg/sqm q 6 weeks, instead of q 3 weeks, after 3 weeks at 700 mg/sqm and 500 mg/sqm, respectively.) Continue therapy until disease progresses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeGAG - 1 g vials.

DATE SUMMARIZED: 02/80

7.0039 PHASE III CTX/BLEO/CACP VS ADR/5-FU/CACP VS MITO/VBL/CACP VS CTX/ADR/CACP FOR METASTATIC NON-SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) EST-2575-IIIR2

OBJECTIVES:

I. Compare the efficacies of 4 combination chemotherapy regimens in the treatment of patients with metastatic non-small cell carcinoma of the lung: cyclophosphamide/bleomycin/cis-platinum vs. adriamycin/5-fluorouracil/cis-platinum vs. mitomycin-C/vinblastine/cis-platinum vs. cyclophosphamide/adriamycin/cis-platinum.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed metastatic non-small cell bronchogenic carcinoma, including adenocarcinoma, epidermoid, and large cell. Patients may not have had prior chemotherapy and must have measurable or evaluable disease. The performance status must be 0-2; kidney, bone marrow, and liver function must be adequate. Patients may not have had prior radiation therapy to the present areas of measurable or evaluable disease nor may they have brain or leptomeningeal disease or symptomatic cardiovascular disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; 5-fluorouracil, 5-FU, NSC-19893; CACP.

Arm III: 3-Drug Combination Chemotherapy. Mitomycin-C, MITO, NSC-26980; Vinblastine, VBL, NSC-49842; CACP.

Arm IV: 3-Drug Combination Chemotherapy. CTX; ADR; CACP.

STRATIFICATION BY: Histologic cell type (epidermoid vs. adenocarcinoma vs. large cell), performance status (0-1 vs. 2).

SPECIAL STUDY PARAMETERS: Performance status, hematologic parameters, kidney and liver function tests, chest x-ray, bone and liver scans, brain scan or CT scan, tumor measurement, EKG, IVP, UGI, bone marrow, skeletal survey.

END POINTS: Response/remission rate, duration of response, objective tumor response.

CURRENT STATUS: Twenty patients will initially be randomized to each treatment arm for each cell type. Thereafter, 5 additional patients will be added to a particular arm for each response seen in the first 20 patients on that arm, to a maximum of 20 additional patients.

DOSAGE SCHEDULE:

Arm I: CTX - 500 mg/sqm iv on days 1 and 8; BLEO - 20 U/sqm iv on days 1 and 8 (maximum dose 30 U); CACP - 30 mg/sqm iv infusion over 30-60 minutes with forced diuresis on days 1 and 8. Repeat courses q 4 weeks and continue until objective evidence of progression.

Arm II: ADR - 25 mg/sqm iv on days 1 and 8; 5-FU - 400 mg/sqm iv on days 1 and 8; CACP - 30 mg/sqm iv infusion over 30-60 minutes with forced diuresis on days 1 and 8. Repeat courses q 4 weeks and continue until objective evidence of progression.

Arm III: MITO - 10 mg/sqm iv push; VBL - 6 mg/sqm iv; CACP - 40 mg/sqm iv infusion over 30-60 minutes with forced diuresis. Repeat courses q 3 weeks until objective evidence of progression.

Arm IV: CTX - 400 mg/sqm iv push; ADR - 40 mg/sqm iv (maximum cumulative dose 450 mg/sqm); CACP - 40 mg/sqm iv infusion over 30-60 minutes with forced diuresis. Repeat courses q 4 weeks and continue until objective evidence of progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MITO - 5 mg vials; VBL - 10 mg ampules; CACP - 10 mg vials; CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; BLEO - 15 U ampules; 5-FU - 500 mg ampules.

DATE SUMMARIZED: 07/80

7.0040 LOCALIZED RADIOTHERAPY WITH VS WITHOUT CAMP (CTX/ADR/MTX/PCB) CHEMOTHERAPY OR HALF-BODY RADIOTHERAPY FOR THORACIC NON-SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) EST-3578

OBJECTIVES:

I. Compare localized chest irradiation vs. localized chest irradiation and CAMP: cyclophosphamide (CTX)/adriamycin (ADR)/methotrexate (MTX)/procarbazine (PCB) chemotherapy vs. localized chest irradiation and half-body irradiation. Evaluation will be based upon a comparison of improvement in performance status, local control within the chest, objective tumor regression, disease-free interval and survival.

II. Compare these three modalities of therapy with regard to normal tissue tolerance toxicity, complications of therapy and their effectiveness to delay or prevent distant metastasis.

PROTOCOL ENTRY CRITERIA: Patients with non-small cell bronchogenic carcinoma proven by biopsy of the primary site or hilar, mediastinal, carinal or supraclavicular lymph nodes, or with repeated positive sputum cytology and serial radiographic evidence of disease. Patients must have disease limited to the thorax and adjacent mediastinal and neurovascular structures and must not have had prior chemotherapy or thoracic radiotherapy. Patients must have adequate bone marrow, renal, hepatic and pulmonary function. Patients must be less than 76 years of age and have an ECOG performance status of 3 or less.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Localized with Cobalt-60, x-ray or linear accelerator.

Arm II: 4-Drug Combination Chemotherapy and Radiotherapy. CAMP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740; Procarbazine, PCB, NSC-77213; plus localized Radiotherapy.

Arm III: Radiotherapy. Localized and half-body exposure.

STRATIFICATION: Participating institutions; performance status: 0 and 1 vs. 2 and 3; extent of disease: limited or extensive (over 2 cm residual disease); histopathology: squamous cell vs. adenocarcinoma and adenosquamous carcinoma vs. large cell anaplastic.

SPECIAL STUDY PARAMETERS: Brain, liver, and bone scans.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival time, disease-free interval, duration of response.

CURRENT STATUS: 100 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Radiotherapy localized to the thorax: 5000 rad continuous irradiation given in 5 weeks. Maximum dose to the spinal column is 4500 rad. Include the primary tumor, mediastinum and both supraclavicular areas in the first 3000 rads given.

Arm II: 3000 rad in 2.5 weeks, including sites as in first 3000 rad of Arm I. Begin Chemotherapy 10 days after completion of Radiotherapy. CAMP: CTX - 300 mg/sqm iv on days 1 and 8; ADR - 20 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on days 1 and 8; MTX - 15 mg/sqm iv on days 1 and 8; PCB - 50 mg (increase 50 mg/day up to 100 mg/sqm; maximum daily dose 200 mg) po on days 2 through 11. Repeat CAMP q 28 days for 6 cycles.

Arm III: Radiotherapy as in Arm II. Begin half-body irradiation 10 days after completion of localized Radiotherapy. 700 rad to the upper half-body, followed by 800 rad to the lower half-body 4 to 6 weeks later after bone marrow recovery.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; MTX - 50 mg vials; PCB - 50 and 100 mg capsules.

DATE SUMMARIZED: 11/79

7.0041 PHASE II CHEMOTHERAPY WITH AMSA FOR METASTATIC OR RECURRENT LUNG CANCER

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PROTOCOL NUMBER(S) NCOG-2N83

OBJECTIVES:

I. Determine the efficacy and toxicity of m-AMSA therapy for patients with metastatic or recurrent lung carcinoma.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with pathologically demonstrated lung cancer with measurable disease parameters. Enter patients with oat cell cancer only after failure of first priority chemotherapy. Patients must have adequate hematologic, liver and kidney function, a Karnofsky performance status (KPS) of 30 or better, and they must not have had any chemotherapy or radiotherapy in the past 3 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: Histological type: squamous cell vs. adenocarcinoma vs. undifferentiated large cell vs. undifferentiated small cell vs. anaplastic unclassified vs. other; extent of disease: limited (T3 or N3 and Mo) vs. extensive N4 or M1); KPS: 80 to 100 vs. 50 to 70 vs. 30 to 40; prior therapy: surgery vs. radiotherapy vs. chemotherapy vs. none.

SPECIAL STUDY PARAMETERS: Liver/spleen, brain and bone scans.

END POINTS: Objective tumor response, response duration, survival time, toxicity/morbidity of treatment, time to progression, response rate.

CURRENT STATUS: A minimum of 7 patients for each major subset will be entered.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv 30 min infusion. Repeat q 3 weeks for a minimum of 2 courses. Continue therapy for responders for 6 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: AMSA - 75 mg vials.

DATE SUMMARIZED: 11/79

7.0042 RADIOTHERAPY WITH NEUTRONS FOR LOCALIZED NONRESECTABLE NON-OAT CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) RTOG-7807

OBJECTIVES:

I. Determine the relative merits of high-LET neutron therapy by evaluation of: the degree of palliative relief attained; the degree and rate of regression in tumor volume; the duration of symptomatic and objective remission; the time of onset and rate of regrowth of recurrent tumor if any; the time of onset, evolution, and severity of radiation injury in surrounding normal lung; and the tumor-free and total survival rates.

II. Determine the dose-time parameters and isoeffect functions for irradiated human lung and for local control of epidermoid, adeno-, adenosquamous, and anaplastic carcinomas in the lung.

III. Determine the toxicity associated with subsequent treatment with systemic chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven malignant tumor of lung or bronchi, including squamous cell or epidermoid carcinomas, adenocarcinomas, and adenosquamous and anaplastic carcinomas; metastases must be limited to supraclavicular nodes. Patients must be without prior chemotherapy and with contralateral lung entirely free of neoplastic disease. Patients must be ambulatory and capable of outpatient visits to the neutron therapy facility.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. High-LET (neutron) therapy.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, disease-free interval, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: Approximately 30 evaluable patients will be entered.

DOSAGE SCHEDULE:

Neutron beam therapy - 1200 rads in 6 divided doses over 3 weeks, midplane dosimetry. Therapy to be initiated within 2 weeks of diagnosis. Subsequent Chemotherapy may be planned or not. Choice of regimen is left to participating institutions; the CAMP combination is recommended.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

7.0043 PHASE III ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE WITH CONCURRENT RADIOTHERAPY FOR UNRESECTABLE LUNG CARCINOMA

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United States of America
PROTOCOL NUMBER(S) RTOG-7811

OBJECTIVES:

I. Determine the effect of radiotherapy with and without immunotherapy with levamisole for unresectable squamous cell carcinoma, undifferentiated large cell carcinoma, and adenocarcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with histologically-proven unresectable squamous cell carcinoma, undifferentiated large cell carcinoma, or adenocarcinoma of the lung in clinical Stage I, Stage II medically inoperable (T1, T2-N0, N1) without mediastinal nodes, or Stage III (T3-N0, N1, T2N1) without mediastinal nodes. (Patients with contralateral hilar nodes are ineligible, per July 1980 revision.) All detectable tumor and regional lymph nodes must be encompassed by radiation therapy fields. Patients must have a performance status of at least 60 and must not have intrathoracic recurrence following curative resection.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus Immunotherapy. Megavoltage irradiation of primary tumor and appropriate lymph nodes; plus Levamisole, LEV, NSC-177023.

Arm II: Radiotherapy plus Placebo.

STRATIFICATION BY: Participating institutions; histologic type: squamous cell vs. undifferentiated large vs. adeno; clinical stage: I or II vs. III; performance status.

SPECIAL STUDY PARAMETERS: Brain and liver scan, skin tests for recall antigens.

END POINTS: Objective tumor response, disease-free interval, response/remission rate, survival time, metastatic pattern, intrathoracic tumor control, immunocompetence.

CURRENT STATUS: 280 patients will be entered in about 3 years.

DOSAGE SCHEDULE: Randomize patients within 28 days after confirmatory diagnostic procedure.

Arm I: Stage I and II - 6000 rad to primary lesion and hilar masses and 4500 rad to hilar and mediastinal nodes in 6 to 7 weeks with 5 fractions/week; Stage III - 5000 rad to tumor and enlarged nodes in 5 to 6 weeks with 5 fractions/week (500 to 1000 rad may be added to gross residual tumor); LEV - 2.5 mg/kg po on days 1 and 2 q week for a maximum of 24 months starting same day as Radiotherapy. Remove patients with progressive disease from study but observe until death.

Arm II: Radiotherapy, as in Arm I, plus placebo.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/76

7.0044 PHASE III PHOTON VS NEUTRON VS PHOTON/NEUTRON RADIOTHERAPY FOR LOCALIZED, INOPERABLE NON-OAT CELL LUNG CANCER

Brady, L., (215-574-3150) Radiation Therapy Oncology Group,
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PROTOCOL NUMBER(S) RTOG-7907

OBJECTIVES:

I. Compare fast neutron teletherapy, both neutrons alone and as part of a mixed beam (neutron/photon), with the best available conventional photon therapy for inoperable non-oat cell lung cancer by evaluating the following: degree and rate of regression of tumor volume; time to onset of tumor regrowth (if any) and rate of regrowth; disease-free survival; absolute survival; time of onset, evaluation and severity of any radiation injury to surrounding normal lung tissue and adjacent critical structures such as heart, esophagus and spinal cord.

PROTOCOL ENTRY CRITERIA: Patients under 80 years old with measurable, histologically proven squamous cell or epidermoid carcinoma, adenocarcinoma, adenosquamous or undifferentiated large cell carcinoma of the lung or bronchi. Patients must have a Karnofsky performance status of 50% or better and must have had neither resection of the primary or prior radiotherapy to the tumor volume and must not have distant metastases.

PROTOCOL OUTLINE: Randomized study.

Arm I: Photon Radiotherapy. Equipment with effective photon energy greater than 1 MeV.

Arm II: Neutron Radiotherapy.

Arm III: Neutron/Photon Mixed Beam Radiotherapy.

STRATIFICATION: Participating institutions; histology: squamous vs. adeno or adenosquamous vs. large cell undifferentiated; primary size: 0-3 cm vs. 3-6 cm vs. over 6 cm; facility for neutron administration.

SPECIAL STUDY PARAMETERS: Liver, bone and brain scans; liver function; bronchoscopy.

END POINTS: Response/remission rate, sympton-free interval, time to symptom relief, time to relapse, survival rate, objective tumor response.

CURRENT STATUS: 240 patients will be entered in 2 years.

DOSAGE SCHEDULE: Begin Radiotherapy within 3 weeks of diagnosis.

Arm I: Photon Radiotherapy - 6000 rad in 6 to 7 weeks to the primary and surrounding tissue.

Arm II: Neutron Radiotherapy - 1800 rad in 6 to 7 weeks to the primary and surrounding tissue.

Arm III: Neutron/Photon Radiotherapy - 3600 rad photon and a minimum of 720 rad neutrons on 6 to 7 weeks to the primary and surrounding tissue.

Follow-up all patients q 2 months for 1 year and then q 4 months until death.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/79

7.0045 PHASE III RADIOTHERAPY VS RADIOTHERAPY PLUS MISONIDAZOLE FOR LOCALLY ADVANCED NON-OAT CELL LUNG CANCER

Brady, L., (215-574-3150) Radiation Therapy Oncology Group,
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United States of America

PROTOCOL NUMBER(S) RTOG-7917

OBJECTIVES:

I. Determine the effects of radiosensitization with misonidazole to radiotherapy for locally advanced Stage III non-oat cell lung cancer.

II. Determine whether potential improvement of intrathoracic tumor control will prolong the disease-free interval and overall survival following radiation therapy.

PROTOCOL ENTRY CRITERIA: Patients between 18 and 70 years of age with clinical Stage III (T1, T2, T3, N2 only), unresectable squamous cell, adeno or undifferentiated large cell lung carcinoma if all the primary tumor and affected regional lymph nodes can be encompassed by radiotherapy fields. Patients must have Karnofsky performance status of at least 60, and adequate bone marrow, liver and kidney function. Patients must not have intrathoracic recurrence following surgery, prior radiotherapy or chemotherapy, prior or concurrent malignancy except non-melanomatous skin cancer, or significant neurological deficit.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Megavolt photons higher than 1 MeV to gross residual tumor and hilar and mediastinal lymph nodes.

Arm II: Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037; plus Radiotherapy, as in Arm I.

STRATIFICATION: Participating institutions; histological type: squamous cell vs. undifferentiated large cell vs. adenocarcinoma; performance status: 60-80 vs. 90-100; disease stage: T1 vs. T2 vs. T3.

SPECIAL STUDY PARAMETERS: Hematologic, liver, and kidney function; MNI plasma level.

END POINTS: Response/remission rate, duration of remission, recurrence rate, recurrence site, toxicity/morbidity of treatment, objective tumor response, length of survival, disease-free interval.

CURRENT STATUS: 200 patients will be entered in about 4 years.

DOSAGE SCHEDULE: Randomize patients 28 days after diagnostic confirmation.

Arm I: 5000 rads in 5 fractions/week for 5 weeks with additional 500-1000 rad boost to residual primary or nodal tumor with reduced fields. An interruption of up to 4 weeks is allowed.

Arm II: MNI - 1.0 g/sqm (maximum total dose 12 g/sqm) po on Monday and Thursday 4 hrs prior to Radiotherapy q week for 5 to 6 weeks. (Revised to 400 mg/sqm daily for 6 weeks, 2 to 4 hours before Radiotherapy, to a total dose not exceeding 12.0 g/sqm. February, 1980.)

Follow patients one month after Radiotherapy, then q 3 months for remainder of year 1, q 4 months for years 2 and 3, then q 6 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 11/79

7.0046 PHASE III RADIOTHERAPY WITH AND WITHOUT MISONIDAZOLE FOR LOCALLY ADVANCED NON-OAT CELL LUNG CANCER

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925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) RTOG-7925

OBJECTIVES:

I. Evaluate the effect of misonidazole (MNI) in enhancing tumor control by irradiation at the primary site and at the regional lymph nodes.

II. Determine whether the potential improvement of intrathoracic tumor control will prolong the disease-free interval and overall survival following radiotherapy.

III. Evaluate the anatomical sites of tumor recurrence following therapy.

IV. Determine whether the addition of MNI modifies the local tumor response to irradiation or the distant dissemination.

V. Evaluate the short-term and late sequelae of radiotherapy combined with MNI.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven, advanced, unresectable squamous cell, undifferentiated large cell, adenocarcinoma of the lung or a cancer of an unknown type. Patients must be between 18 and 75 years old, have a Karnofsky performance status of 60 or better and adequate bone marrow, hepatic and renal function. Patients must have no prior chemotherapy nor radiotherapy. (Patients who have received chemotherapy more than 4 weeks prior to entry are eligible, per July 1980 revision.)

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037. Radiotherapy with megavoltage equipment to the primary lesion and bilar and mediastinal lymph nodes.

Arm II: Radiotherapy. As in Arm I.

STRATIFICATION BY: Participating institutions; disease type: squamous vs. adeno, undifferentiated large cell, unknown; disease stage: T1, T2, T3-N3 vs. T4; performance status: 60-80 vs. 90-100.

SPECIAL STUDY PARAMETERS: CT scan of primary tumor.

END POINTS: Survival rate, disease-free interval, recurrence rate, objective tumor response, toxicity/morbidity of treatment, duration of response.

CURRENT STATUS: 200 patients to be entered over 4 years.

DOSAGE SCHEDULE:

Arm I: MNI - 1.75 g/sqm (maximum cumulative dose 10.5 g/sqm) po twice q week. Repeat for 3 courses. Begin Radiotherapy 4 hours after MNI, 3600 rad in 3 weeks.

Arm II: Radiotherapy. 3600 rad in 3 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 02/80

7.0047 PHASE III POSTOPERATIVE RADIOTHERAPY WITH/WITHOUT LEVAMISOLE IMMUNOTHERAPY FOR NON-OAT CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) RTOG-7927

OBJECTIVES:

I. Evaluate the hypothesis that the addition of non-specific immune stimulation in the form of levamisole delays or reduces the appearance of distant metastasis following definitive surgery and postoperative radiation therapy for non-oat cell carcinoma of the lung.

II. Evaluate the hypothesis that the addition of non-specific immune stimulation in the form of levamisole delays or reduces local recurrence of tumor following surgery and postoperative radiation therapy for non-oat cell carcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of bronchogenic carcinoma, either squamous cell, adeno-, or large cell undifferentiated carcinoma. Surgical removal of primary tumor by wedge resection, lobectomy, bilobectomy, or pneumonectomy must have been performed; no gross known intrathoracic disease must remain. There must be no metastases beyond the mediastinum. Patients must have recovered from surgery and be started on radiation therapy within 60 days and have a reasonable expectation for adequate follow-up for at least one year. Karnofsky performance status of not less than 40 is required, and age must be between 18 and 75 years.

PROTOCOL OUTLINE: Randomized, single-blind study.

Arm I: Radiotherapy plus Immunotherapy. Megavoltage (Co-60, 2 MeV x-rays or 4 MeV linear accelerator); plus Levamisole, LEV, NSC-177023.

Arm II: Radiotherapy plus placebo.

STRATIFICATION BY: Participating institutions; extent of surgery: wedge resection vs. bilobectomy or lobectomy vs. pneumonectomy; histology: squamous cell carcinoma, any grade vs. adenocarcinoma, any grade vs. large cell undifferentiated carcinoma; disease stage: 2 vs. 3.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, duration of response, disease-free interval, length of survival, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 125 patients will be entered. An accrual rate of 100 patients per year is anticipated.

DOSAGE SCHEDULE:

Arm I: 5000 rads total dose to tumor delivered in daily fractions of 180-200 rads for 5 days/week for 5 weeks. LEV - 2.5 mg/kg po on days 1 and 2 weekly, starting with the first dose of radiation therapy. Continue until evidence of toxicity or for 1 year.

Arm II: 5000 rads total dose to tumor as in Arm I. Placebo given in same form and schedule as LEV in Arm I.

All patients will be followed every 3 months during first year, and every 6 months thereafter up to 5 years, then yearly. An additional radiation booster dose of 1000 rads may be given at the discretion of the radiation therapist.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

7.0048 PHASE II PILOT STUDY OF PALA CHEMOTHERAPY FOR ADVANCED BRONCHOGENIC CARCINOMA

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PROTOCOL NUMBER(S) SEG-LUN-P41

OBJECTIVES:

I. Determine whether PALA is effective in inducing responses in advanced bronchogenic carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with progressive, measurable and histologically diagnosed squamous, adeno, large or small cell bronchogenic carcinoma not eligible for curative surgery, radical radiotherapy or higher priority protocols. Patients must have a Karnofsky performance status of 40% or more and have recovered from previous myelosuppressive therapy. Patients with small cell bronchogenic carcinoma must be refractory to protocols SEG-76LUN309, SEG-78LUN328 or to combination chemotherapy with adriamycin, cyclophosphamide with or without vincristine. Patients must have normal renal function, creatinine less than 2, and adequate liver and hematologic function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Serum creatinine.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response.

CURRENT STATUS: 14 to 30 patients will be entered in 18 months.

DOSAGE SCHEDULE:

PALA - 4 gm/sqm iv infused over 30 to 60 min q 7 days for 8 weeks. Repeat for 8 more weeks for responders. Remove nonresponders from study. Escalate PALA to 6 gm/sqm for the second 8 weeks therapy. Continue PALA as long as tumor responds or until toxicity intervenes.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 10 mg ampules.

DATE SUMMARIZED: 11/79

7.0049 PHASE III ADJUVANT IMMUNOTHERAPY WITH C. PARVUM AND LEVAMISOLE AND RADIOTHERAPY FOR INOPERABLE LUNG CARCINOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-76LUN0203; SEG-76LUN308

OBJECTIVES:

I. Determine whether immunotherapy with C. parvum, employed as adjunctive therapy to radiotherapy, will prevent or delay recurrence (prolongation of disease-free interval) and improve survival (prolongation of survival) when compared to the effect of radiotherapy alone.

II. Determine whether adjunctive immunotherapy with levamisole will prolong the disease-free interval and improve survival following radiotherapy.

III. Determine the effect of adjuvant immunotherapy upon the patient's immune status as measured by tests in vivo and in vitro.

PROTOCOL ENTRY CRITERIA: Patients who have histologically proven (including cytology) lung cancer of the following histologic types: squamous cell carcinoma, adenocarcinoma and undifferentiated large celi carcinoma.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Megavoltage irradiation (Co-60, 2 MeV x-ray, or 4 MeV linear accelerator) plus placebo.

Arm II: Adjuvant Immunotherapy plus Radiotherapy. Corynebacterium parvum (Burroughs-Wellcome), C. parvum, NSC-220537.

Arm III: Immunotherapy plus Radiotherapy. Levamisole, LEV, NSC-177023.

STRATIFICATION BY: Participating institution, histology type (adenocarcinoma, undifferentiated carcinoma, large cell carcinoma); disease stage (Stage I, II-inoperable or III) and TNM categories based on clinical and radiographic information. When surgical findings are available include scalene node biopsy, mediastinoscopy or exploratory thoracotomy staging.

SPECIAL STUDY PARAMETERS: Alkaline phosphatase, bilirubin, BUN, creatinine, LDH, SGOT total protein and albumin, C. parvum antibody levels and complement. Recall skin antigens, DNCB; immunoglobulin quantitation.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, immunologic parameters before and after immunotherapy.

CURRENT STATUS: 864 patients will be entered.

DOSAGE SCHEDULE:

Arm I: For Stage I-II disease, give primary lesion 6000-6500 rads total dose and give hilar and mediastinal lymph nodes 5000 rads total dose divided into 4 to 6 fractions/week over 6 to 7 weeks. For Stage III disease give primary lesion, hilar and mediastinal nodes 4000-5000 rads tumor dose divided into 4 to 5 fractions/week over 6 to 7 weeks. Placebo will be prepared by NCI to resemble LEV, and be administered using same route and schedule.

Arm II: C. parvum - 0.2 mg/sqm iv on day 1; 0.5 mg/sqm iv on day 3; 1.0 mg/sqm iv on day 5; 2 mg/sqm on day 7 and weekly thereafter for a total of 5 doses at the same level; then give 4 mg/sqm sc in 4 divided doses administered to 4 injection sites, every other week. Begin Radiotherapy on day 7.

Arm III: LEV - 2.5 mg/kg po on days 1 and 2 once a week until relapse. Radiotherapy as in Arm I beginning on day 7.

Evaluate Immunotherapy dosage after 1 year.

Dosage modifications for toxicity are given as indicated by wbc and platelet count and side effects of radiotherapy.

DOSAGE FORMS: C. parvum - 5 ml vials; LEV - 50 mg tablets.

DATE SUMMARIZED: 01/77

PATIENT ACCRUAL: 00361078

7.0050 PILOT PHASE II STUDY OF CAP (CYCLOPHOSPHAMIDE/ADRIAMYCIN/CIS-PLATINUM) FOR ADENOCARCINOMA OF THE LUNG

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group,
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35294, United States of America
PROTOCOL NUMBER(S) SEG-77PLUN0302

OBJECTIVES:

I. Determine the response rate, complete and partial, of a combination of adriamycin, cyclophosphamide and cis-platinum in patients with adenocarcinoma of the lung.

II. Determine the toxicity of responses to this regimen.

PROTOCOL ENTRY CRITERIA: Ambulatory patients with metastatic large cell adenocarcinoma, with a life expectancy greater than 1 month. Patients may not have congestive heart failure or renal disease.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. CAP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Liver and bone scans, audiogram, EKG.

END POINTS: Objective tumor response, response rate, survival.

CURRENT STATUS: About 27 patients will be entered.

DOSAGE SCHEDULE:

CTX - 400 mg/sqm iv; ADR - 40 mg/sqm iv; CACP - 40 mg/sqm iv. Repeat course q 4 weeks for 10 courses. Palliative Radiotherapy may be given. Remove from study patients with progression after 2 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials, 50 mg tablets; CACP - 10 mg vials; ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 07/78

7.0051 PHASE III CAMF VS CAP-I VS CTX/ADR THERAPY FOR ADVANCED SQUAMOUS, LARGE CELL OR ADENOCARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) SEG-78LUN326R; SEG-78LUN326; SEG-78LUN0103

OBJECTIVES:

I. Determine which of 3 chemotherapy regimens: CAMF: cyclophosphamide (CTX)/adriamycin (ADR)/methotrexate (MTX)/citrovorum factor (CF), CAP-I: CTX/ADR/cis-platinum (CACP) or CA: CTX/ADR has a higher response rate in the treatment of advanced non small cell carcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with cytologically or histologically confirmed measurable squamous cell, undifferentiated large cell or adenocarcinoma of the lung, Stage IV including T-4 with any N, N-3 with any T, M of any category or advanced Stage III not eligible for radical Radiotherapy (Protocol SEG 76LUN0203). Patients must have adequate blood counts, renal and cardiac function and a Karnofsky performance status of at least 50%. Patients must not have had prior therapy with ADR, CTX, MTX, or CACP and must have had 2 weeks rest since prior palliative Radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

Arm II: 3-Drug Combination Chemotherapy. CTX; ADR; cis-Platinum, CACP, NSC-119875.

Arm III: 2-Drug Combination Chemotherapy. CTX, ADR. (Revision, December 1978).

STRATIFICATION BY: Histologic type: squamous vs. adenocarcinoma vs. undifferentiated large cell; prior radiotherapy; Karnofsky performance status: 80 to 90% vs. 60 to 70% vs. 50%.

SPECIAL STUDY PARAMETERS: Renal and hepatic function tests, EKG, audiogram.

END POINTS: Response/remission rate, disease progression, objective tumor response, survival rate, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: 270 patients will be entered in about 2 to 2 1/2 years.

DOSAGE SCHEDULE:

Arm I: CTX - 500 mg/sqm iv on day 1 (maximum single dose 1000 mg); ADR - 50 mg/sqm iv on day 1 (maximum single dose 100 mg, maximum cumulative dose 450 mg/sqm); MTX - 400 mg/sqm po in 4 divided doses on day 1; if toxicity permits, escalate to 800 mg/sqm for subsequent courses; CF - 20 mg po or im in 4 divided doses on day 2 plus 10 mg in 2 divided doses (given q 6 hours) on day 3.

Arm II: CTX - 400 mg/sqm iv on day 1; ADR - 40 mg/sqm iv day 1; CACP - 40 mg/sqm iv on day 1. Escalate CTX to 480 mg/sqm and ADR to 48 mg/sqm in subsequent courses if hematologic toxicity permits.

Arm III: CTX - 500 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1 (maximum cumulative dose 450 mg/sqm).

Repeat courses in all 3 Arms q 21 days for 3 courses. Give 5 additional courses to responders and follow for response duration. Remove patients with disease progression from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; MTX - 2.5 and 50 mg tablets; CTX - 100, 200 and 500 mg vials; CF - 3 mg ampules, 5 mg tablets; CACP - 10 mg vials.

DATE SUMMARIZED: 06/79

PATIENT ACCRUAL: 00130978

7.0052 PHASE III CHEMOTHERAPY WITH FOMI (5-FU/VCR/MITO) VS CAP (CTX/ADR/CACP) VS FOMI/CAP FOR ADVANCED ADENO- AND LARGE CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) SWOG-8012

OBJECTIVES:

I. Evaluate by pairwise comparison the response rate, duration of response and survival of three regimens: FOMi: 5-fluorouracil (5-FU), vincristine (VCR) and mitomycin-C (MITO); CAP: adriamycin (ADR), cyclophosphamide (CTX) and cis-platinum (CACP); and combined FOMi/CAP in patients with advanced TMN Stage III M1 adenocarcinoma and large cell undifferentiated carcinoma of the lung.

II. Evaluate the degree of non-cross resistance of FOMi in CAP failures and of CAP in FOMi failures.

III. Compare the toxicities and side effects of FOMi and CAP.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed diagnosis of adenocarcinoma or large cell undifferentiated carcinoma of the lung with measurable and/or evaluable disease. (Alveolar cell carcinoma is also acceptable.) Patients with metastatic disease are eligible, including patients with metastases to the opposite lung or supraclavicular nodes. Patients whose disease can be encompassed within a single radiation port are not eligible. There must be no prior chemotherapy; any prior radiotherapy must have failed to prevent disease progression to Stage III M1. The performance status must be 30 or better on the Karnofsky scale. There must be no history of serious heart disease; the creatinine level must be below 1.5 mg percent for men and below 1.2 mg percent for women unless creatinine clearance is greater than 60 cc/minute. Patients with liver impairment are eligible but will require drug dose reduction.

PROTOCOL OUTLINE: Randomized study. Alveolar cell cancer patients go to Arm I only.

Arm I: 3-Drug Combination Chemotherapy. FOMi: 5-Fluorouracil, 5-FU, NSC-19893; Vincristine, VCR, NSC-67574; Mitomycin-C, MITO, NSC-26980.

Arm II: 3-Drug Combination Chemotherapy. CAP: Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; cis-Platinum, CACP, NSC-119875.

Arm III: 3-Drug Sequential Combination Chemotherapy. FOMi followed by CAP.

STRATIFICATION BY: Participating institutions; histological grade: adenocarcinoma vs. large cell carcinoma; performance status: 0-1 vs. 2-3; bone or brain involvement: yes vs. no.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; x-rays or scans of measurable lesions.

END POINTS: Response/remission rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 261 patients will be entered in 2.5 years.

DOSAGE SCHEDULE:

Poor-risk patients (those with inadequate bone marrow reserve) receive reduced drug doses shown in parentheses.

Arm I: FOMi: 5-FU - 300 (200) mg/sqm iv bolus on days 1 through 4; VCR - 2.0 (1.0) mg/sqm iv on day 1; MITO - 10 (5) mg/sqm iv on day 1. Repeat q 3 weeks for 3 courses, then q 6 weeks. If after 2 courses CR, PR or stable disease status is not achieved, cross over to Arm II.

Arm II: CAP: CTX - 400 (200) mg/sqm iv on day 1; ADR - 40 (20) mg/sqm iv on day 1; CACP - 40 (40) mg/sqm iv on day 1. Repeat q 4 weeks. If after 2 courses CR, PR or stable disease status is not achieved, cross over to Arm I.

Arm III: FOMi: 5-FU, VCR and MITO as in Arm I; 4 weeks later give CAP: CTX, ADR and CACP as in Arm II. Repeat sequence q 8 weeks.

Patients must receive at least one course of FOMi and one course of CAP for an adequate trial. Patients with progressive disease after adequate trial go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules; CTX - 50 mg tablets; 5-FU - 500 mg ampules; MITO - 5 mg vials, VCR - 1 and 5 mg ampules; CACP - not given.

DATE SUMMARIZED: 10/80

7.0053 PHASE III COMBINATION CHEMOTHERAPY WITH ADR/CACP VS ADR/CACP/VP-16 FOR SQUAMOUS CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) SWOG-8015

OBJECTIVES:

I. Determine the activity, in terms of response rate, remission duration, and survival in patients with extensive squamous cell (epidermoid) carcinoma of the lung, for two combination chemotherapy programs: adriamycin (ADR)/cis-platinum (CACP) versus VP-16213 (VP-16)/ADR/CACP.

II. Assess the feasibility and reliance of applying 'measurable versus evaluable' criteria of tumor regression in determining therapeutic response.

III. Correlate tumor grade with response and survival.

IV. Evaluate the relative toxicities of these respective regimens.

PROTOCOL ENTRY CRITERIA: Patients of any age with extensive squamous cell (epidermoid) lung carcinoma, TNM system Stage III. Patients must not have received prior chemotherapy or immunotherapy. Lesions must be either evaluable or measurable. There must no evidence of uncontrolled angina, arrhythmia or congestive heart failure, and renal function must be within acceptable limits. Blood chemistry and liver function must be acceptable.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy. ADR; CACP; VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: Disease stage: measurable vs. evaluable; prognostic risk: good vs. poor.

SPECIAL STUDY PARAMETERS: Bone marrow biopsy; IVP; creatinine clearance; cardiac scan; hematologic, renal and hepatic function tests.

END POINTS: Response/remission rate, duration of response, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 210 patients will be entered in 2.5 years.

DOSAGE SCHEDULE:

Arm I: ADR - 30 mg/sqm iv 5-minute infusion on days 1 and 8, followed by CACP - 50 mg/sqm iv infusion at rate of 1 mg/minute. Prior to CACP infusion, patient should receive 2 liters of fluid either po or iv. Repeat course q 28 days.

Arm II: ADR - 25 mg/sqm iv 5-minute infusion on days 1 and 8, followed by CACP - 50 mg iv infusion as in Arm I; VP-16 - 80 mg/sqm iv infusion over 30-60 minutes, preceeding ADR and CACP on days 1 through 3. Repeat course q 28 days.

Poor-risk patients (those with performance status 2-4 and those over 65 years of age) will be treated initially at 66 percent of doses stated above. Repeat courses contingent upon creatinine clearance, WBC and platelet counts. Patients with progressive or unacceptable stable disease after one course go off study. Those who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CACP - 10 mg vials; VP-16 - 100 mg vials.

DATE SUMMARIZED: 10/80

7.0054 PHASE I-II EVALUATION OF LUNG AND WHOLE BRAIN RADIOTHERAPY PLUS CHEMOTHERAPY (5-FU/MITO/VCR) FOR LIMITED ADENO AND LARGE CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) SWOG-8068

OBJECTIVES:

I. Determine the toxicity of 5-fluorouracil/mitomycin-C/vincristine plus simultaneous radiotherapy to the primary and to the brain in patients with localized, inoperable adeno and large cell carcinoma of the lung.

II. Evaluate in these patients the effectiveness of combination radiotherapy to the primary chest tumor and draining lymph node areas plus combination chemotherapy in terms of response, duration of response, and patient survival.

PROTOCOL ENTRY CRITERIA: Patients with inoperable, limited, histologically proven adenocarcinoma or large cell carcinoma of the lung who have not received previous radiotherapy or chemotherapy and who have a performance status of 3 or less by SWOG criteria. Evidence of absence of systemic metastasis must be documented by negative pretreatment physical examination, bone scan, brain scan, and liver/spleen scan. Renal function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Radiotherapy. Co-60 or 2-6 MeV external beam generators.

Regimen B: 3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Mitomycin-C, MITO, NSC-26980; Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Performance status (0-1 vs. 2-3), tumor size (greater or less than 4 cm), cell type (large cell vs. adenocarcinoma), weight loss during the 12 months prior to entry (less than 12 percent vs. 12 percent or greater), age (more than 70 years vs. not more than 70 years), supraclavicular node involvement (yes vs. no).

SPECIAL STUDY PARAMETERS: Hematologic parameters, renal and hepatic function tests, electrolytes, chest x-ray, bone scan, brain scan, liver/spleen scan, other x-rays as indicated.

END POINTS: Response/remission rate, objective tumor response, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 14-25 patients will be required for the study.

DOSAGE SCHEDULE:

Regimen A: Whole Brain Radiotherapy - total dose of 4125 rads to the whole brain through parallel opposed lateral fields in 10 daily fractions of 275 rads each, followed by 2 weeks of rest, followed by 5 more identical fractions. Treatment to begin on day 1. Primary Tumor Area Radiotherapy - total dose of 5400 rads to the primary area in the chest delivered as follows: 11 fractions of 200 rads/day followed by 2 weeks rest followed by 11 additional identical fractions; followed by a boost dose of 1000 rads delivered only to the areas where the initial tumor was present. Treatment to begin on day 1.

Regimen B: 5-FU - 500 mg/sqm iv bolus on days 1 and 8; VCR - 1 mg/sqm (maximum 2 mg) iv bolus on day 1; MITO - 5 mg/sqm iv bolus on day 1. Begin Chemotherapy within 4 days of start of Radiotherapy and repeat courses q 28 days for 3 courses. Then repeat at 42-day intervals at these dosages: MITO - 10 mg/sqm iv bolus on day 1; VCR - 1 mg/sqm (maximum 2 mg) on day 1; 5-FU - 500 mg/sqm iv bolus on days 1, 8, and 15. After 8 cycles of Chemotherapy, reevaluate CR and PR for subsequent treatment decision.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg ampules; MITO - 5 mg vials; VCR - 1 and 5 mg ampules.

DATE SUMMARIZED: 12/80

7.0055 PHASE II CHEMOTHERAPY WITH MAYTANSINE FOR SQUAMOUS CELL CARCINOMA OF THE LUNG

Lichtenfeld, K. M., (301-528-7912) Baltimore Cancer Research Program, Baltimore, Maryland, United States of America

PROTOCOL NUMBER(S) BCRP-7708

OBJECTIVES:

I. Evaluate the effectiveness of maytansine in the treatment of inoperable squamous cell carcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven nonresectable and/or metastatic squamous cell carcinoma of the lung with an expected survival time exceeding 2 months. Prior surgery must have been completed 4 weeks before study entry, prior radiotherapy must have been restricted to limited areas for symptomatic control. Adequate hematological, liver and kidney functions and a performance status of 3 or less (Zubrod scale) are required.

PROTOCOL OUTLINE:

Single-agent Chemotherapy. Maytansine, MTS, NSC-153858.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: SMA-12, CEA, bone survey, liver-spleen scan, CAT-scan of the head.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response, survival time, survival rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

MTS - 0.5 mg/sqm/day iv on days 1, 2 and 3. Repeat course q 21 days for a minimum of 2 courses. Continue therapy for responders and patients with stable disease until clear progression. Remove from study patients with progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 04/78

7.0056 CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE AND DIMETHYLSULFOXIDE FOR METASTATIC EPIDERMOID CARCINOMA OF THE LUNG

Aisner, J., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America

PROTOCOL NUMBER(S) BCRP-7713

OBJECTIVES:

I. Determine the feasibility of combining cyclophosphamide and dimethylsulfoxide in patients with metastatic epidermoid carcinoma of the lung.

II. Develop toxicity data from this combination of drugs.

III. Determine whether this combination of drugs affects the response rate, duration of response, or survival in patients with disseminated epidermoid lung cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented metastatic epidermoid carcinoma of the lung who have measurable disease other than pleural effusions and mixed osteoblastic/osteolytic bone lesions. Patients must be less than 60 years old and ambulatory. Bone marrow, hepatic, and renal functions must be adequate and there must be no other malignant tumors.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Potentiation. Cyclophosphamide, CTX, NSC-26271; Dimethylsulfoxide, DMSO, NSC-763.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Chest x-ray, whole lung tomograms, hematologic parameters, liver and kidney function tests, CEA, isotope scanning as indicated, ophthalmologic evaluation.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

CTX - 1500 mg/sqm iv on day 3; DMSO - 2000 ml of 2 percent solution po on days 1 and 2 and 1000 ml on day 3. Repeat course q 21 days. Give at least 2 courses before declaring failure, and treat responders and those with stable disease until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/80

7.0057 CYCLOPHOSPHAMIDE PLUS WHOLE-BODY HYPERTHERMIA FOR ADENOCARCINOMA AND LARGE CELL CARCINOMA OF THE LUNG

Van Echo, D. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7819

OBJECTIVES:

I. Determine the therapeutic efficacy of whole-body hyperthermia plus cyclophosphamide in patients with advanced adeno or large cell carcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven adeno or large cell carcinoma of the lung that is metastatic and not amenable to surgery or aggressive local radiotherapy. Patients must have measurable disease and must not have had prior exposure to cyclophosphamide. Patients must have reasonable pulmonary status, adequate liver and bone marrow function, and no evidence of coronary artery disease. Patients must be under 60 years of age and have a Karnofsky performance status of at least 50 percent. There may be no brain metastases nor massive liver metastases.

PROTOCOL OUTLINE: Nonrandomized study.

Whole-body Hyperthermia plus Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: Karnofsky status (80-100 percent vs. 50-70 percent), weight loss (greater or less than 10 percent of body weight).

SPECIAL STUDY PARAMETERS: Chest x-rays, whole lung tomograms, hemogram, SMA-12 and creatinine.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Hyperthermia at 41.8 degrees C. for 4 hours; CTX - 1.5 g/sqm iv infusion during hyperthermia. Evaluate for toxicity at 21 days. Repeat course q 21 days if toxicity is acceptable; give at least 2 courses before declaring failure. Treat responders for 1 year or until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

7.0058 COMBINATION CHEMOTHERAPY WITH CTX/ADR/VP-16 WITH AND WITHOUT CACP FOR ADVANCED NON-SMALL CELL CANCER OF THE LUNG

Ostrow, S., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7907

OBJECTIVES:

I. Determine the feasibility of administering the combination cyclophosphamide/adriamycin/VP-16/cis-platinum and develop toxicity data for this combination.

II. Determine whether this combination can augment the response rate, response duration, or survival in patients with disseminated non-small cell carcinoma of the lung.

III. Determine whether moderate-dose cis-platinum can augment the response of patients with non-small cell carcinoma of the lung to combination chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented non-small cell carcinoma of the lung that is metastatic and not amenable to surgery. Patients must have measurable disease and may not have received prior cytotoxic therapy. Patients must be ambulatory and have normal renal and hepatic function and bone marrow reserves. There may be no history of any other primary malignant neoplasm or recent myocardial infarction.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; VP-16213, VP-16, NSC-141540.

Arm II: 4-Drug Combination Chemotherapy. CTX; ADR; VP-16; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Prior radiation therapy (treatment vs. no treatment), Karnofsky performance status (0 vs. 1 vs. 2 vs. 3 vs. 4), participating institutions.

SPECIAL STUDY PARAMETERS: Chest x-ray, whole-lung tomograms, liver and brain scans, bone scans or bone surveys, hematologic parameters, bone marrow biopsy, liver function tests, CEA, EKG, 24-hour urine for creatinine and protein, calculated creatinine clearance.

END POINTS: Response/remission rate, duration of response, objective tumor measurement, toxicity/morbidity of treatment.

DOSAGE SCHEDULE:

Arm I: CTX - 800 mg/sqm iv over 1 hour on day 1; ADR - 45 mg/sqm iv push on day 1, total cumulative dose not to exceed 540 mg/sqm; VP-16 - 100 mg/sqm over 1 hour on days 1, 3, and 5. Repeat course q 21 days. Substitute Methotrexate at 40 mg/sqm when maximum dose of ADR has been reached.

Arm II: CTX, ADR, and VP-16 as in Arm I; CACP - 40 mg/sqm iv over 3 hours. Repeat course q 21 days.

Give at least 2 courses before declaring failure. Responding patients should be treated continuously until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

7.0059 DAVA WITH AND WITHOUT CIS-PLATINUM FOR ADVANCED NON-SMALL CELL CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) BCRP-7915

OBJECTIVES:

I. Determine the rate and duration of response and the toxicities of vindesine (DAVA) when used as a single agent in patients with advanced non-small cell carcinoma of the lung.

II. Determine whether cis-platinum can improve the rate and duration of response to DAVA in patients with advanced non-small cell carcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven non-small cell carcinoma of the lung that is metastatic, measurable, and not amenable to surgery. Hematologic parameters must be adequate, and renal and hepatic function must be normal. There may be no prior history of another primary malignant neoplasm.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with prior therapy with cis-Platinum to Regimen A and those with no prior cis-Platinum to Regimen B.

Regimen A: Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

Regimen B: 2-Drug Combination Chemotherapy. DAVA; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Prior radiotherapy vs. no prior radiotherapy; prior treatment with CACP vs. no prior CACP; Karnofsky performance status (normal vs. ambulatory vs. less than 50 percent of time in bed vs. more than 50 percent of time in bed vs. bedridden).

SPECIAL STUDY PARAMETERS: Chest x-ray, whole-lung tomograms, metastatic bone survey, isotope scans as indicated, hematologic parameters, liver and kidney function tests, CEA, EKG, audiogram, creatinine clearance, nerve conduction tests.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

DOSAGE SCHEDULE:

Regimen A: DAVA - 3 mg/sqm/week iv for 6 doses, then q 2 weeks.

Regimen B: DAVA as in Regimen A; CACP - 100 mg/sqm/month iv with adequate pre- and post-hydration and concomitant mannitol diuresis.

Minimum duration of treatment will be 8 weeks. Responders continue on treatment until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

7.0060 ADJUVANT BCG/INH/LEV IMMUNOTHERAPY VS CAP-I (CTX/ADR/CACP) FOR STAGE II AND III LARGE CELL AND ADENOCARCINOMA OF THE LUNG

McGuire, W. P., (301-496-2522) Lung Cancer Study Group, 7910 Woodmont Ave., Room C804, c/o Natl. Canc. Inst., Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) LCSG-772; MDAR-261

OBJECTIVES:

I. Compare combination chemotherapy (CAP-I) versus combination immunotherapy with BCG/isoniazide (INH)/levamisole (LEV) for their ability to prolong the survival and increase the cure rate of patients with completely resected Stage II and III large cell adenocarcinoma of the lung.

II. Compare the two treatment regimens for their effects on patterns of disease recurrence and metastases.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with apparently totally resected Stage II or III large cell, undifferentiated or adenocarcinoma of the lung, with adequate bilirubin, creatinine and hematologic levels. Amended in Addendum 2, April 1980 to exclude any prior thoracic radiotherapy, chemotherapy, or immunotherapy within the past 5 years and prior history of any other cancer unless there has been a 5-year disease-free interval. Patients must be staged at surgery, must not have any distant metastases, other neoplasms, recently active tuberculosis or active cardiac disease (defined in Addendum 2, April 1980, as a myocardial infarction within 4 months or any ventricular arrythmia requiring medication).

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-B116327; Isoniazide, INH, NSC-9659; Levamisole, LEV, NSC-177023. For fever: Aspirin, NSC-27223; plus Benadryl, NSC-33299.

Arm II: 3-Drug Combination Chemotherapy. CAP-I: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions; arrythmia vs. no arrythmia; disease stage: II vs. III; more vs. less than 10% weight loss prior to surgery.

SPECIAL STUDY PARAMETERS: Optional immune and skin tests; sputum cytology; liver, bone and brain scans; pulmonary function; EM study.

END POINTS: Toxicity/morbidity of treatment, evidence of recurrence or metastases, disease-free interval, survival, recurrence site, recurrence rate.

CURRENT STATUS: 156 patients will be entered in 1.7 years.

DOSAGE SCHEDULE:

Arm I: Between day 4 and day 10 after surgery, give BCG - 1 cc (day 14, as per Addendum 1, September 1978) suspension containing 10 to the seventh power viable organisms given as a single dose intrapleurally by thoracentesis for patients who have had a pneumonectomy, via chest tube for patients who have had a lobectomy. Treat ensueing fever with Aspirin - 600 mg, and Benadryl -as needed. LEV - 2.5 mg/kg po on days 1, 2 and 3 q 2 weeks for 18 months. Beginning 14 days after BCG dose, give INH - 300 mg/day po for 12 weeks.

Arm II: Between day 22 and day 30 after surgery, give on day 1: (day 42, as per Addendum 1, September 1978) CTX - 400 mg/sqm iv; ADR -40 mg/sqm iv; CACP - 40 mg/sqm iv. Repeat q month for a total of 6 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCG - ampules containing 5 times 10 to the eighth colony forming units; INH - 300 mg tablets; LEV - 50 mg tablets; CTX -200 and 500 mg vials; ADR - 10 and 50 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 00360279

7.0061 ADJUVANT RADIOTHERAPY WITH OR WITHOUT LEVAMISOLE IMMUNOTHERAPY FOR EPIDERMOID CARCINOMA OF THE LUNG, STAGES II AND III

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PROTOCOL NUMBER(S) LCSG-773; MDAR-263

OBJECTIVES:

I. Determine if postoperative adjuvant therapy in the form of levamisole and/or radiation therapy will prolong the disease-free interval and prolong the survival of patients with resectable Stage II and III epidermoid lung carcinoma in comparison to those patients treated with surgery alone.

II. Compare the three regimens for their effects on patterns of disease recurrence.

PROTOCOL ENTRY CRITERIA: Patients with totally resected epidermoid carcinoma of the lung, Stage II or III, staged at surgery with extent of disease fully documented, with margins and intrathoracic region microscopically free of tumor, no known metastases beyond the mediastinum and no prior therapy with levamisole or prior (clarified as within 5 years, Addendum 4, April 1980) thoracic radiotherapy, chemotherapy or immunotherapy. Patients should have no prior history of any other cancer (other than non-melanoma skin cancer or in-situ cervical cancer) unless a 5-year no-treatment disease-free interval exists. Eligible surgical staging includes Stages II - T2N1M0, Stage III - any TN2M0, T3N0M0, T3N1M0.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Megavoltage.

Arm II: Radiotherapy plus Immunotherapy. Levamisole, LEV, NSC-177023.

Arm III: Control. No further therapy.

STRATIFICATION BY: Participating institutions; disease stage: II vs. III; weight loss prior to surgery: more vs. less than 10%; age: greater vs. less than 60.

SPECIAL STUDY PARAMETERS: Electron microscopy for diagnosis if necessary; PPD - at least 48 hours prior to surgery; sputum cytology; node biopsies; liver, brain and bone scans as indicated.

END POINTS: Disease-free interval, response/remission rate, site of recurrence, survival time, survival rate.

CURRENT STATUS: About 318 patients will be entered in about 3 1/2 years.

DOSAGE SCHEDULE:

Arm I: Beginning between 28 and 42 days (56 days, as per Addendum 1, September 1978), after surgery, give 5000 rad (plus or minus 10%. Patients receiving less than 4500 rad should be followed but will be considered to have received an inadequate trial of radiation. As per Addendum 1, September 1978), in 5 weeks to the mediastinum and involved fields.

Arm II: Radiotherapy as in Arm I, plus LEV - 2.5 mg/kg/day on days 1, 2 and 3 q 14 days for a total of 18 months. Begin LEV as close as possible to the 4th day after surgery and not after the 10th postsurgical day. Monitor wbc q 4 weeks.

Arm III: Not applicable.

Evaluate all patients 4 to 6 weeks following surgery, at 12 weeks and q 3 months thereafter for 2 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: LEV - 50 mg tablets.

DATE SUMMARIZED: 04/78

PATIENT ACCRUAL: 00460279

7.0062 CAP-I CHEMOTHERAPY VS RADIOTHERAPY VS BOTH MODALITIES FOR PARTIALLY RESECTED LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) LCSG-791; MDAR-362

OBJECTIVES:

I. Compare effects of chemotherapy with CAP-I: cyclophosphamide (CTX)/adriamycin (ADR)/cis-platinum (CACP) vs. CAP-I plus thoracic irradiation vs. thoracic irradiation alone for local and systemic control of incompletely resected non-small cell bronchogenic carcinoma.

II. Determine which therapy prolongs survivorship in patients with macroscopic vs. microscopic residual disease.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with documented, non-small cell carcinoma of the lung who have incompletely resected macroscopic or microscopic residual disease confined to the surgically treated hemithorax. Patients ineligible for protocols LCSG 772 and 773 because of positive most proximal node group are eligible because of presumed microscopic residual disease. Patients must have adequate pulmonary function for planned radiotherapy, adequate hematologic, liver, and kidney function, and a Karnofsky performance status of at least 50. Patients must not have had any prior thoracic radiotherapy, chemotherapy, or immunotherapy (within the past 5 years, Addendum 2, April 1980), active cardiac disease, or pleural effusion with positive cytology.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I, II, or III 3 to 5 weeks after surgery.

Arm I: 3-Drug Combination Chemotherapy. CAP-I: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy plus Radiotherapy. CAP-I, plus megavolt irradiation of primary tumor and mediastinal lymph nodes.

Arm III: Radiotherapy. Megavolt irradiation, as in Arm II.

STRATIFICATION: Participating institutions; cell type: squamous (epidermoid) vs. non-squamous (adeno and large cell); residual disease: microscopic vs. macroscopic: Karnofsky performance status: 50 to 70 vs. 80 to 100%.

SPECIAL STUDY PARAMETERS: Pulmonary function; liver, brain, and bone scans; sputum cytology; bronchoscopy.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival rate.

CURRENT STATUS: 375 to 500 patients will be entered in 3 or 4 years.

DOSAGE SCHEDULE: Begin therapy within one week of randomization.

Arm I: CAP-I: CTX - 400 mg/sqm, ADR - 40 mg/sqm, CACP - 40 mg/sqm, all given iv on day 1 q 4 weeks for 6 courses.

Arm II: CAP-I, as in Arm I; radiotherapy beginning on day 1; 2000 rad/week in 5 daily fractions given in weeks 1 and 5 concurrent with first 2 courses of CAP-I to primary tumor and mediastinal lymph nodes.

Arm III: 2000 rads in 5 fractions/week for 2 courses starting within 1 week of randomization with 3 weeks of rest between courses.

Keep patients on study until recurrence or disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 200 and 500 mg vials; ADR - 10 and 50 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 11/79

7.0063 COMBINATION CHEMOTHERAPY WITH CAP-I (CTX/ADR/CACP) VS NO THERAPY FOR COMPLETELY RESECTED NON-SMALL CELL LUNG CARCINOMA

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PROTOCOL NUMBER(S) LCSG-801

OBJECTIVES:

I. Compare the effect of combination chemotherapy with CAP-I: cyclophosphamide (CTX), adriamycin (ADR) and cis-Platinum (CACP) vs. no treatment on the rates of recurrence and survival in patients with completely resected T1NS and T2NO non-small cell lung cancer.

II. Compare the two treatment regimens for the effects on patterns of disease recurrence and metastasis.

III. Compare the two treatments for toxicity.

PROTOCOL ENTRY CRITERIA: Patients no more than 75 years of age with surgically resectable carcinoma of the lung (squamous, adenocarcinoma and large cell). Small cell carcinoma is excluded. Patient must have been staged at surgery and extent of the disease fully documented; the tumor must have been fully or totally resected. There must be no active cardiac disease or distant metastases. Recovery from surgery must be sufficiently rapid to permit therapy no later than 30 days postoperative.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. CAP-I: Cyclophosphamide (Cytoxan), CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Arm II: No treatment.

STRATIFICATION BY: Histology: squamous vs. nonsquamous or mixed; preoperative WBC: equal to or less than 9100 vs. greater than 9100; performance status, preoperative: equal to or less than 9 vs. 10; participating institutions.

SPECIAL STUDY PARAMETERS: SGOT, EKG, sputum cytology, mediastinoscopy, mediastinal node biopsy.

END POINTS: Response/remission rate, survival rate, length of survival, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 225 patients will be entered in 2.5 years.

DOSAGE SCHEDULE:

Arm I: CAP-I: CTX - 400 mg/sqm iv on day 1 q 3 weeks; ADR - 40 mg/sqm iv on day 1 q 3 weeks; CACP - 60 mg/sqm iv on day 1 q 3 weeks. Drugs will be given as rapid injection via the side arm of a freely running iv using 500 ml of 5 percent D/one-half NS. After the agents are administered, an additional 1000 ml of 5 percent D/one-half NS plus 25 g mannitol will be given over 2 hours. Patients receive a total of four 1-day treatments, the first to begin between 14 and 30 days post-surgery, and are followed thereafter until death or until loss to followup.

Arm II: No treatment. Patient followup begins 14 to 30 days after Surgery; it continues q 3 weeks for 3 months, then q 3 months for 2 years postoperative, then q 6 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 200 and 500 mg vials; ADR - 10 and 50 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 12/80

7.0064 T-CAP (TZT/CTX/ADR/CACP) VS FAM (5-FU/ADR/MITO) COMBINATION CHEMOTHERAPY FOR ADENOCARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) MAYO-782102

OBJECTIVES:

I. Evaluate the combination chemotherapy regimen of FAM: 5-fluorouracil (5-FU)/adriamcyin (ADR)/mitomycin-C (MITO) in adenocarcinoma of the lung.

II. Compare the efficacy of FAM vs. T-CAP: Triazinate (TZT)/cyclophosphamide (CTX)/ADR/cis-Platinum (CACP).

PROTOCOL ENTRY CRITERIA: Patients with measurable or evaluable disease of histologically or cytologically confirmed, surgically or radiotherapeutically incurable Stage III adenocarcinoma of the lung and patients with Stage I or Stage II adenocarcinoma of the lung medically unable to undergo surgical or radiation therapy. Patients must have adequate hematological and cardiac status, creatinine below 1.5 mg/dl, a performance status better than 4, no prior treatment with the present chemotherapy nor prior combination chemotherapy. At least 3 weeks must have elapsed since major surgery and 4 to 6 weeks must have elapsed since prior monochemotherapy. Patients must not have had radiotherapy within the past 30 days to more than 15% of the bone marrow.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. T-CAP: Triazinate, TZT, NSC-139105; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy. FAM: 5-Fluorouracil, 5-FU, NSC-19893; ADR; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION BY: Performance status: 0 to 1 vs. 2 to 3; measurable vs. evaluable tumor.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, response/remission rate, recurrence rate, toxicity/morbidity of treatment, response duration.

CURRENT STATUS: 160 patients will be entered.

DOSAGE SCHEDULE:

Arm I: T-CAP: TZT - 150 mg/sqm iv infusion on day 1; CACP - 20 mg/sqm iv infusion following TZT on days 1, 2 and 3; ADR - 40 mg/sqm iv push before TZT on day 2; CTX - 400 mg/sqm iv push before TZT on day 3. Repeat course every 4 weeks until disease progression.

Arm II: FAM: 5-FU - 600 mg/sqm iv push on days 1, 8, 29, 36; ADR - 30 mg/sqm iv push on days 1, 29; MITO - 10 mg/sqm iv push on day 1. Repeat course every 8 weeks until disease progression. Give no more than the maximum total ADR dose (450 mg/sqm) to non-cardiac disease patients; continue therapy in responders with remaining drugs. Give palliative radiotherapy selectively.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; ADR - 10 and 50 mg vials; CACP - 10 mg vials; TZT - 100 and 250 mg vials; 5-FU - not given; MITO - 5 mg vials.

DATE SUMMARIZED: 07/79

7.0065 CAP-I (CTX/ADR/CACP) VS V-CAP-I (CTX/ADR/CACP/VP-16) VS T-CAP (CTX/ADR/CACP/TZT) PLUS RADIOTHERAPY FOR NONRESECTABLE NON-SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) MAYO-792401

OBJECTIVES:

I. Compare the regression rates of a 3-drug combination, CAP-I: cyclophosphamide (CTX)/adriamycin (ADR)/cis-platinum (CACP) to that of two 4-drug combinations, T-CAP: CTX/ADR/CACP/Baker's antifol (TZT) and V-CAP-I: CTX/ADR/CACP/VP-16213 (VP-16).

II. Compare CAP-I plus thoracic radiotherapy to V-CAP-I and T-CAP plus radiotherapy from the standpoints of time to progression, sites of progression and survival.

PROTOCOL ENTRY CRITERIA: Patients less than 73 years of age with histologically or cytologically confirmed, nonresectable, non-small cell lung cancer. Patient must have adequate cardiac and pulmonary function and an ECOG performance status better than 4. Patient must have disease confined to one hemithorax and the supraclavicular fossae, and must not have had prior radiation or chemotherapy, no prior lobectomy within 3 weeks or pneumonectomy within 4 weeks.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Thoracic Radiotherapy (TRT). CACP-I: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875. Radiotherapy with a 4 or 10 MeV linear accelerator.

Arm II: 4-Drug Combination Chemotherapy plus Radiotherapy. T-CAP: CTX; ADR; CACP; Baker's Antifol, TZT, NSC-139105. TRT as in Arm I.

Arm III: 4-Drug Combination Chemotherapy plus Radiotherapy. V-CAP: CTX; ADR; CACP; VP-16213, VP-16, NSC-141540. TRT as in Arm I.

STRATIFICATION: Cell type: adenocarcinoma vs. squamous cell vs. large cell or mixed; age: under 60 vs. above 60; sex, supraclavicular or scalene nodal involvement; thoracic disease: unresected vs. incompletely resected.

SPECIAL STUDY PARAMETERS: Bone and liver scan, bronchoscopy.

END POINTS: Response/remission rate, objective tumor response, duration of response, time to progression, survival.

CURRENT STATUS: 100 patients will be entered in 2 years.

DOSAGE SCHEDULE: Enter all patients within 6 weeks of initial diagnosis.

Arm I: CAP-I: ADR - 40 mg/sqm iv on day 1; CTX - 400 mg/sqm iv on day 3; CACP - 20 mg/sqm iv on days 1 through 3. Repeat CAP-I, in patients with no disease progression after 4 weeks, then 4 weeks after the second course begin patients without progression on ADR, CTX as above; CACP - 8 mg/sqm iv on days 1 through 5, given 1 to 3 hours after radiation dose. TRT - 2000 rad in 5 days to the primary, hilar and mediastinal nodes and involved supraclavicular fossae. Repeat course with TRT after 4 weeks in patients without progression, then repeat 3-day CAP-I course without TRT 4 weeks later if no progression.

Arm II: T-CAP: ADR, CTX, CACP as in CAP-I; TZT - 150 mg/sqm iv on days 1 through 3. Repeat T-CAP in patients with no progression after 4 weeks. 4 weeks later, continue patients without progression on ADR, CTX as in CAP-I; CACP - 8 mg/sqm iv on days 1 through 5; TZT - 125 mg/sqm iv on days 1 through 3 plus TRT as in Arm I. If no disease progression appears, repeat this 5-day course with TRT after 4 weeks. Repeat T-CAP course without TRT in 4 weeks if no disease progression appears.

Arm III: V-CAP: ADR, CTX, CACP as in CAP-I; VP-16 - 60 mg/sqm iv on days 1 through 3. Repeat V-CAP in patients without progressive disease after 4 weeks. Continue patients after 4 weeks with no progression on ADR, CTX, as in CAP-I; CACP - 8 mg/sqm iv on days 1 through 5, VP-16 - 60 mg/sqm iv on days 1 through 3 plus TRT as in Arm I. If no disease progression appears, repeat 5-day V-CAP course with TRT in 4 weeks. Continue 3-day V-CAP course without TRT in 4 more weeks if no disease progression appears.

Remove patients with disease progression in any Arm at any time from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200 and 500 mg vials; VP-16 - 100 mg ampules; CACP - 10 mg vials; TZT - 100 and 250 mg vials.

DATE SUMMARIZED: 11/79

7.0066 CHEMOTHERAPY WITH CTX, ADR, CACP, MITO FOR ADVANCED NON-SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) MAYO-792407

OBJECTIVES:

I. Compare effect of CAP: cyclophosphamide (CTX) adriamycin (ADR) cis-platinum (CACP) vs. CAP followed by CAP alternating with CTX/ADR vs. MAP: mitomycin-C (MITO)/ADR/CACP followed by MAP alternating with ADR/CACP for non-small cell lung cancer.

PROTOCOL ENTRY CRITERIA: Patients up to 74 years of age with histologically - or cytologically confirmed, measurable or evaluable, non-small cell cancer of the lung with disease beyond one hemithorax, ipsilateral hilum, ipsilateral and central mediastinum and both supraclavicular fossae (includes ipsilateral pleural effusion with positive cytology, bloody characteristics, or protein at least 3 gm). Patients must have: adequate hematologic and kidney function, normal liver function, ECOG performance status of at least 3. Patients must not have chemotherapy or major surgery in prior 3 weeks or prior chemotherapy with nitrosoureas.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. CAP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy alternating with 2-Drug Combination Chemotherapy. CAP alternating with CTX; ADR.

Arm III: 2-Drug alternating Combination Chemotherapy. MAP: Mitomycin-C, MITO, NSC-26980; CACP. Alternate with ADR; CACP.

STRATIFICATION BY: Performance status: 0 or 1 vs. 2 or 3; cell type: adeno vs. large vs. squamous vs. mixed; tumor grade: 4 vs. 3 or 2 vs. unknown; age: under 70 vs. 70 or over.

SPECIAL STUDY PARAMETERS: Tumor measurement, kidney function, bone and liver scan.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 180 patients in 2 years.

DOSAGE SCHEDULE:

Arm I: CTX - 400 mg/sqm iv push on day 1; ADR - 40 mg/sqm iv push on day 1; CACP - 60 mg/sqm iv over 2 hrs in 1000 ml D5W/1/2 NS plus 25 gm mannitol on day 1; q 4 weeks until progression.

Arm II: CAP: as in Arm I for 2 courses, then alternate q 4 weeks with CTX/ADR - as in Arm I, until progression.

Arm III: MAP: MITO - 8 mg/sqm (10 mg/sqm in alternating part of therapy) iv push on day 1; ADR and CACP as in Arm I; q 4 weeks for 2 courses, then alternate q 4 weeks with ADR/CACP as in Arm I, until progression.

Remove from study patients in progression during first 2 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, 500 mg vials, ADR - 10 and 50 mg vials; CACP - 10 mg vials; MITO - 5 mg vials.

DATE SUMMARIZED: 02/80

7.0067 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED LUNG CANCER

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-802501

OBJECTIVES:

I. Evaluate N-(phosphonacetyl)-L-aspartate (PALA) in the treatment of patients with advanced lung cancer.

PROTOCOL ENTRY CRITERIA: Patients with a histologic or cytologic diagnosis of lung cancer and advanced disease (Stage III unresectable or metastatic), not currently eligible for combination chemotherapy because of medical condition or prior treatment. Cell types included: large cell; squamous cell; adenocarcinoma; mixed; small cell. Patient must have measurable or evaluable disease and no prior surgery within 3 weeks or chemotherapy within 4 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION BY: Age: less or more than 70 years old; performance status; prior chemotherapy.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 20 Regimen A and 15 Regimen B patients will be accrued in approximately 6 months and slightly more than a year, respectively. If none of the first 15 patients in Regimen A shows regression, study will be terminated.

DOSAGE SCHEDULE:

PALA - 6.0 g/sqm (5.0 g/sqm for patients over 70 years of age, those with a PS of 3, prior chemotherapy, or a serum creatinine value 1.6-2.0 mg/dl) iv infusion over 2 hours on day 1, repeated after 3 weeks, then every 4 weeks. Repeat, if regression or stable, with appropriate dose modifications. If progression is noted, patient goes off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 1000 mg vials.

DATE SUMMARIZED: 05/80

7.0068 PHASE II CHEMOTHERAPY WITH DON FOR METASTATIC OR RECURRENT LUNG CANCER

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PROTOCOL NUMBER(S) MAYO-802502

OBJECTIVES:

I. Conduct a Phase II study of 6-diazo-5-oxo-L-norleucine (DON) in patients with metastatic or recurrent lung cancer.

II. Document any toxicities, both acute and chronic, from the repeated use of DON.

PROTOCOL ENTRY CRITERIA: Patients with histologic or cytologic diagnosis of metastatic or recurrent lung cancer. There must be measurable or evaluable disease; all cell types are included. Patients must be less than 75 years of age and have an ECOG performance status better than 4. There must be adequate hematologic, renal and hepatic function. Patients must not undergo major surgery or receive chemotherapy within 3 weeks of entry (6 weeks for nitrosoureas, hexitol, or mitomycin-C).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. 6-Diazo-5-oxo-L-norleucine, DON, NSC-7365.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Tumor measurements; PA chest x-ray; hematologic, renal, and hepatic function tests.

END POINTS: Objective tumor response, response rate, toxicity/morbidity of treatment.

CURRENT STATUS: This study will accrue approximately 60 patients over a 6-month period.

DOSAGE SCHEDULE:

DON - 160 mg/sqm iv infusion over 10 minutes on days 1, 2, and 3. Thirty minutes prior to DON infusion, 7.5 mg/sqm of Compazine, an antiemetic, is given im. Patients are retreated after a 3-week interval; subsequently, patients are retreated at 4-week intervals. Patients showing regression and those with stable disease continue treatment. Patients with progressive disease go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DON - 100 mg vials.

DATE SUMMARIZED: 01/81

7.0069 NUTRITIONAL SUPPORT FOR PATIENTS ON PROTOCOL MDAR-102 CHEMOTHERAPY AND IMMUNOTHERAPY FOR METASTATIC LUNG CARCINOMA

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PROTOCOL NUMBER(S) MDA-DT-7623

OBJECTIVES:

I. Evaluate whether better tumor response (qualitatively and quantitatively) can be achieved by maintaining patients in positive caloric balancce.

II. Evaluate whether hyperalimented patients could tolerate larger doses of antineoplastic agents.

III. Evaluate whether optimal nutritional support alters the rate of tumor growth.

IV. Evaluate whether adequate nutritional support modifies the host-immune response.

V. Evaluate the toxicities associated with the prolonged administration of intravenous hyperalimentation.

PROTOCOL ENTRY CRITERIA: Patients with measurable lesions of histologically proven metastatic carcinoma of the lung of the non oat cell variety who are to initiate remission induction chemoimmunotherapy with Protocol MDA-DT-7609 (MDAR-102).

PROTOCOL OUTLINE: Randomized Study for patients with no more than 24% weight loss. Enter all patients with more than 24% weight loss to Arm I and analyze separately.

Arm I: Intravenous Hyperalimentation (IVH), prior to and during Chemoimmunotherapy.

Arm II: Control. No IVH. Chemoimmunotherapy only.

STRATIFICATION BY: Participating institutions; sex; weight status compared to patient's usual weight: weight loss none to 6% vs. 6 to 12% vs. 12 to 24% vs. more than 24%; disease category.

SPECIAL STUDY PARAMETERS: Historical and present dietary intake; serum proteins; electrolytes; immunoglobulins; glycemia; serum iron, iron binding capacity; creatinine excretion; triceps skinfold and arm circumference measurements; lymphocyte cultures; skin tests; labeling index of tumor cells, daily weight.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, quality of response to chemoimmunotherapy and correlation with changes in anthropometric, metabolic and immunologic parameters.

CURRENT STATUS: 40 patients in each disease category will be entered over a period of 2 years.

DOSAGE SCHEDULE:

Arm I: IVH via subclavian catheter for 4.5 weeks. Begin IVH 10 days before start of chemotherapy - 1000 cc on day 1 containing 500 ml 50% dextrose, plus 500 ml 8.5% amino acid solution with additives: 40-50 milliequivalents (mEq) sodium chloride, 20 mEq potassium acetate, 15 mEq potassium acid phosphate, 15 mEq magnesium sulfate, 15 ml multivitamins (MVI) and 1 gm calcium gluconate. Establish and improve tolerance to glucose load, then give 3000 cc (about 3000 calories) per day in 3 1000 cc iv drips given over 8 hours each. Add MVI only once a day to one 1000 cc bottle. Perform daily calorie counts (po and iv) and clinical studies (see Special Study Parameters) on days 0, 10, and 32 of IVH. Remove patients from study if disease progresses after a minimum of 2 4.5-week courses.

Arm II: No IVH. Study extent of disease for 10 days before start of chemoimmunotherapy. Perform clinical evaluations as in Arm I.

Modification of the amount of calories to be administered will be done by the investigating hyperalimentation physician.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/79

7.0070 PHASE II CHEMOTHERAPY WITH PALA, BRUCEANTIN OR VINDESINE FOR NON-OAT CELL LUNG CANCER

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PROTOCOL NUMBER(S) MDAR-328; MDA-DT-7903

OBJECTIVES:

I. Determine the efficacy of PALA, bruceantin (BRU) and vindesine (DAVA), each administered alone, in patients with metastatic non-oat cell lung cancer.

II. Determine the qualitative and quantitative toxicities of each of these drugs by the intravenous route administered on the following schedules: PALA on a single-dose schedule, BRU on a 5-day schedule, and DAVA on a 5-day continuous infusion schedule.

III. Determine duration of response and duration of survival of patients receiving each of these treatments.

PROTOCOL ENTRY CRITERIA: Ambulatory patients over 15 years of age with histologically proven measurable lesions or evaluable disease of metastatic non-oat cell lung cancer. Patients must not have had prior chemotherapy and must be off all prior immunotherapy or radiotherapy for at least 4 weeks and must have recovered from all toxic effects of such therapy. Patients must have a life expectancy of at least 12 weeks and they must have adequate bone marrow, liver and renal functions. Enter patients with inadequate bone marrow and abnormal liver function as poor-risk patients (PRP).

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. PALA, NSC-245467.

Arm II: Single-agent Chemotherapy. Bruceantin, BRU, NSC-165563.

Arm III: Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: Histologic type: squamous cell vs. adenocarcinoma.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Objective tumor response, response/remission rate, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 90 patients will be entered, 30 patients in each Arm.

DOSAGE SCHEDULE:

Arm I: PALA - 5 g/sqm iv single dose q 2 weeks if toxicity permits.

Arm II: BRU - 3.5 mg/sqm/day (2.5 mg for poor-risk patients) iv on days 1 through 5 q 3 to 4 weeks depending on recovery from toxicity.

Arm III: DAVA - 1.2 mg/sqm/day (1 mg for poor-risk patients) iv continuous 24-hour infusion on days 1 through 5 q 2 weeks if toxicity permits.

Give a minimum of 2 courses on each arm for an adequate trial and continue therapy for a total period of 2 years or 1 year after achievement of complete response, whichever is shorter. Adjust dosages of all drugs according to hematologic toxicities observed. Remove from study patients with increasing disease after 2 courses or patients developing unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DAVA - 10 mg ampules; PALA - 1.0 g ampules; BRU - 3.0 mg vials.

DATE SUMMARIZED: 09/79

7.0071 CAP-1 (CYCLOPHOSPHAMIDE/ADRIAMYCIN/CIS-PLATINUM) CHEMOTHERAPY PLUS RADIOTHERAPY FOR NON-OAT CELL LUNG CANCER

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PROTOCOL NUMBER(S) MDAR-335; MDA-DT-7915

OBJECTIVES:

I. Improve response rate and survival of patients with locally advanced non-oat cell lung cancer over that of historical controls.

II. Prolong the disease-free interval and survival of patients with early lung cancer.

III. Evaluate the curative potential and the toxicities associated with this approach.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven Stage I, II, or III limited non-oat cell lung cancer. Patients with residual or medically nonresectable disease or with superior sulcus tumors are eligible. Patients must have a minimum life expectancy of 12 weeks, no prior chemotherapy and adequate bone marrow, hepatic and renal function. Any prior therapy must have been terminated 4 weeks prior to entry, with recovery from toxic effects.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Radiotherapy. CAP-I: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875, plus Cobalt-60 or supervoltage radiation.

Arm II: 3-Drug Combination Chemotherapy plus Radiotherapy. Supervoltage radiation as in Arm I plus prophylactic brain irradiation plus CAP-I as in Arm I.

STRATIFICATION: Cell type, disease stage.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, survival rate, disease-free interval, toxicity/morbidity of treatment, objective tumor response, survival time.

CURRENT STATUS: 75 patients will be entered in 4-5 years.

DOSAGE SCHEDULE:

Arm I: Enter all patients within 3 to 4 weeks after surgery, if performed. CAP-I: CTX - 500 mg/sqm iv on day 1; ADR - 50 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on day 1; CACP - 12 mg/sqm iv on days 1 through 4. Repeat course q 3 weeks as toxicity permits, until maximum dose of ADR is reached. Radiotherapy. Omit for patients with prior radiotherapy. 5000 rads in 5 weeks to the chest beginning with the 3rd CAP-I course, with dose reduction to CTX - 100 mg/sqm; ADR - 10 mg/sqm; CACP - 10 mg/sqm during radiotherapy.

Arm II: CAP-I plus Radiotherapy as in Arm I, plus 3000 rad in 2 weeks to the brain given concurrently with chest radiotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

7.0072 COMBINATION CHEMOTHERAPY WITH FAM (5-FLUOROURACIL/ADRIAMYCIN/MITOMYCIN-C) FOR NON-RESECTABLE ADENOCARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) MDAR-339; MDA-M2/gm32

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with FAM: 5-fluorouracil (5-FU)/adriamycin (ADR)/mitomycin-C (MITO) in adenocarcinoma of the lung.

II. Assess the value of an intensive induction phase of FAM chemotherapy in patients with untreated and previously treated adenocarcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically or cytologically proven, unresectable adenocarcinoma of the lung. Patients must have a minimum life expectancy of 10 weeks and must have no prior exposure to the study agents. Patients must have adequate hematologic, renal, hepatic and cardiac function.

PROTOCOL OUTLINE: Nonrandomized study.

Induction and Maintenance: 3-Drug Combination Chemotherapy. FAM: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Mitomycin-C, MITO, NSC-26980.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 25 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Induction: 5-FU - 600 mg/sqm iv on days 1 through 3; ADR - 25 mg/sqm (maximum cumulative dose 550 mg/sqm, 450 mg/sqm for patients at risk for developing ADR cardiotoxicity) iv on days 1 through 3; MITO - 10 mg/sqm iv on day 1. Repeat course on day 31, then enter patients to Maintenance after a 28 day rest.

Maintenance: 5-FU - 600 mg/sqm iv on days 1 and 2; ADR - 25 mg/sqm iv on days 1 and 2; MITO - 10 mg/sqm iv on day 1 beginning with the third course. Repeat course q 21 days twice excluding MITO. Repeat cycle of 3 courses, with MITO given only q third course, for 18 months.

Dosage modifications for toxicity and prior therapy are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

7.0073 PHASE II CHEMOTHERAPY WITH PCNU FOR METASTATIC LUNG CANCER OF ALL TYPES REFRACTORY TO FIRST LINE CHEMOTHERAPY

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PROTOCOL NUMBER(S) MDAR-385; MDA-DT-8006

OBJECTIVES:

I. Determine the efficacy of PCNU administered by iv infusion at 6-8 week intervals to patients with metastatic lung cancer of all types.

II. Determine the quantitative and qualitative toxicity of this treatment.

III. Determine the duration of response and survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic lung cancer of all types who have failed on higher priority treatment programs. Patients with brain metastases need not have had prior treatment. Patients must have a life expectancy of at least 12 weeks, measurable lesions, and adequate marrow, kidney, and liver function. Patients must be at least 15 years of age and must be off all previous chemotherapy, immunotherapy, or radiotherapy for at least 4 weeks before entering the study. There must be no residual toxicity from prior therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PCNU, NSC-95466.

STRATIFICATION BY: Prior Mitomycin-C therapy (yes vs. no), prior extensive radiotherapy (yes vs. no), bone marrow status.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment, survival rate.

CURRENT STATUS: A minimum of 30 evaluable patients will be entered.

DOSAGE SCHEDULE:

PCNU - 100 mg/sqm iv infusion. Repeat at 6-8 week intervals depending on recovery from previous toxicities. Patients with inadequate bone marrow reserve or with prior Mitomycin-C treatment or extensive radiotherapy will begin treatment at 60 mg/sqm. Treatment will continue for 2 years or for 1 year after achieving CR, whichever is shorter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

7.0074 RADIOTHERAPY PLUS COMBINATION CHEMOTHERAPY WITH CEP (CTX/VP-16/CACP) VS CAP (CTX/ADR/CACP) FOR LIMITED NON-OAT CELL LUNG CANCER

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PROTOCOL NUMBER(S) MDAR-386; MDA-DT-8007

OBJECTIVES:

I. Compare the response, duration of response, and survival of patients with limited adenocarcinoma and squamous cell carcinoma of the lung when treated with radiotherapy combined with cyclophosphamide/cis-platinum/adriamycin or with cyclophosphamide/cis-platinum/VP-16213.

II. Compare the toxicities of these two regimens quantitatively and qualitatively.

III. Evaluate the role of prophylactic brain irradiation in the prevention of CNS metastases.

PROTOCOL ENTRY CRITERIA: Adult patients with histologic proof of limited non-small cell lung carcinomas. Patients must not have malignant pleural effusions and may not have previously been treated with radiotherapy or chemotherapy. Patients must have a life expectancy of at least 12 weeks and must have measurable lesions. Bone marrow, hepatic, and renal functions must be adequate.

PROTOCOL OUTLINE: All patients enter Regimen A Induction, where they are randomized to Arms I and II. Patients in CR or PR following Induction are evaluated for the possibility of surgical resection, Regimen B; stable patients proceed directly to Regimen C, where they are randomized to Arms III and IV. Patients then resume Regimen A Chemotherapy on the arm to which they were initially randomized.

Regimen A: Induction.

Arm I: 3-Drug Combination Chemotherapy. CEP: Cyclophosphamide, CTX, NSC-26271; cis-Platinum, CACP, NSC-119875; VP-16213, VP-16, NSC-141540.

Arm II: 3-Drug Combination Chemotherapy. CAP: CTX; CACP; Adriamycin, ADR, NSC-123127.

Regimen B: Surgery. Resection of residual tumor.

Regimen C:

Arm III: Radiotherapy plus 3-Drug Combination Chemotherapy. Chest irradiation plus CEP or CAP as in Arm I or Arm II.

Arm IV: Radiotherapy plus 3-Drug Combination Chemotherapy plus Prophylactic Radiotherapy. Chest irradiation plus CEP or CAP as in Arm I or Arm II plus prophylactic whole brain irradiation.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 60 evaluable patients will be entered over a 2-year period.

DOSAGE SCHEDULE:

Regimen A: Induction.

Arm I: CEP: CTX - 500 mg/sqm iv on day 1; VP-16 - 70 mg/sqm iv on days 1 through 3; CACP - 80 mg/sqm iv on day 1. Repeat for a total of 3 courses at intervals of 3-4 weeks.

Arm II: CAP: CTX - 500 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; CACP - 80 mg/sqm iv on day 1. Repeat for a total of 3 courses at intervals of 3-4 weeks.

Regimen B: Surgical resection of residual tumor.

Regimen C:

Arm III: Radiotherapy - 5000 rads/5 weeks to the mediastinum and both supraclavicular areas. CTX - 100 mg/sqm iv; VP-16 - 40 mg/sqm iv for CEP patients only; ADR - 10 mg/sqm iv for CAP patients only; CACP - 15 mg/sqm iv. Repeat weekly throughout Radiotherapy.

Arm IV: Radiotherapy as in Arm III plus 3000 rads/2 weeks to the whole brain. Chemotherapy as in Arm III, throughout Radiotherapy.

Following completion of Regimen C therapy, patients resume Regimen A Chemotherapy for 4 additional courses on the arm to which they were initially randomized.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

7.0075 PHASE II COMBINATION CHEMOTHERAPY WITH CACP/VP-16 FOR EXTENSIVE NON-OAT CELL LUNG CANCER

Valdivieso, M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-402; MDA-DT-8033

OBJECTIVES:

I. Determine the efficacy in terms of remission rate, remission duration, and survival for the combination of VP-16213 and cis-platinum when administered in a 4-day intravenous schedule to patients with adenocarcinoma and squamous cell lung cancer.

II. Determine the toxicities associated with the administration of these agents in this fashion.

PROTOCOL ENTRY CRITERIA: Adult patients with histologically proven non-oat cell (adenocarcinoma, squamous, large cell and bronchoalveolar histologies) lung cancer of the extensive disease category. Patients must have measurable disease and a life expectancy of at least 12 weeks; renal, hepatic and hematologic functions must be adequate. Patients must have no prior chemotherapy; those with prior radiotherapy and/or surgery must show clear evidence of disease progression.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. VP-16213, VP-16, NSC-141540; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests.

END POINTS: Response/remission rate, remission duration, survival, objeective tumor response.

CURRENT STATUS: 28 patients will be entered, 14 in each major histologic subtype: squamous and adenocarcinoma.

DOSAGE SCHEDULE:

CACP - 80 mg/sqm on day 1; VP-16 - 100 mg/sqm on days 2, 3 and 4. Repeat Chemotherapy at 3-week intervals.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

7.0076 PHASE II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR METASTATIC LUNG CANCER

Valdivieso, M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-405; MDA-DT-8031

OBJECTIVES:

I. Determine the efficacy of anthracenedione (dihydroxyanthracenedione) administered by a 5-day intravenous schedule to patients with metastatic lung cancer.

II. Determine the qualitative and quantitative toxicity of anthracenedione administered in this fashion.

III. Determine the duration of response and duration of survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of metastatic lung cancer of all histologies who have failed on protocol treatments of higher priority. Patients must have measurable lesions. Patients must be at least 15 years of age and have adequate bone marrow, liver, and renal function. Patients must have been off all previous chemotherapy, immunotherapy, or radiotherapy for the 4 weeks prior to entry and must have recovered from the toxic effects of that therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Anthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests.

END POINTS: Response/remission rate, duration of response, objective tumor response.

CURRENT STATUS: 14 evaluable patients in each major subtype (squamous, adenocarcinoma, and oat cell carcinoma) will be entered.

DOSAGE SCHEDULE:

DHAD - 4 mg/sqm iv daily for 5 days q 4 weeks. Poor-risk patients receive 3 mg/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

7.0077 PHASE II EVALUATION OF HUMAN LEUKOCYTE INTERFERON IN ADVANCED NON-SMALL CELL LUNG CANCER

Krown, S. E., (212-794-7426) Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York, 10021, United States of America

PROTOCOL NUMBER(S) MSKCC-7952

OBJECTIVES:

I. Determine the activity of human leukocyte interferon at two dosage levels in patients with advanced non-small cell lung cancer.

II. Determine the effect of interferon on immune function.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed non-small cell lung cancer who have measurable disease that has not previously been irradiated. Patients must be no older than 70 years, must have a PS of at least 50, and must have adequate hematologic parameters. No therapy, including steroids, may be administered in the preceding 4 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy. Human Leukocyte Interferon.

STRATIFICATION BY: Point of entry into study: first 15 patients vs. subsequent patients.

SPECIAL STUDY PARAMETERS: Bone marrow aspirate for CFU-c and cell cycle kinetic studies; biochemical screening profile; 5-prime nucleotidase; gamma-glutamyl transpeptidase; CEA; DNCB sensitization and challenge and intradermal skin tests with microbial antigens; appropriate scans; assay for natural killer cell activity; lymphocyte surface markers and T cell subpopulations; serum immunoglobulin levels; viral antibody titers; expression of HLA antigens on peripheral blood lymphocytes and measurement of HLA antibodies; stimulation of lymphocytes with mitogens and antigens; measurement of interferon in serum and urine.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response.

CURRENT STATUS: At least 14-19 patients are expected to be entered into the study.

DOSAGE SCHEDULE:

The initial 15 patients receive Interferon - 3 x 10 to the sixth units/day im for 30 days. Subsequent patients receive Interferon - 10 x 10 to the sixth units/day im for 30 days. Give no additional antitumor therapy for 30 days after Interferon therapy. Observe CR or PR without additional therapy until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/80

7.0078 DAVA/CACP/BLEO COMBINATION CHEMOTHERAPY VS METHYL-GAG SINGLE-AGENT CHEMOTHERAPY FOR NON-SMALL CELL LUNG CANCER

Gralla, R. J., (212-794-8382) Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York, 10021, United States of America

PROTOCOL NUMBER(S) MSKCC-8017

OBJECTIVES:

I. Evaluate the efficacy of vindesine, cis-platinum, and bleomycin in previously treated patients (with PS values 80 percent or higher) with non-small cell lung cancer.

II. Evaluate the efficacy of methyl-GAG in previously treated and untreated patients with non-small cell lung cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically or cytologically confirmed non-small cell lung cancer, measurable disease that has not been previously irradiated. Patients must be under 70 years of age; they must have a creatinine clearance greater than or equal to 65, a NY Heart Association Class I or II cardiac status, and adequate hematologic function. Patients who have and have not received prior chemotherapy must have PS values of at least 60 and 80 percent, respectively.

PROTOCOL OUTLINE: Randomized study. Patients are randomized to Arm I or Arm II. Patients with progressive disease after 6 weeks on either arm will be crossed over.

Arm I: 3-Drug Combination Chemotherapy. Vindesine, DAVA, NSC-245467; cis-Platinum, CACP, NSC-119875; Bleomycin, BLEO, NSC-125066.

Arm II: Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

STRATIFICATION BY: Prior treatment: yes vs. no; epidermoid vs. non-epidermoid.

SPECIAL STUDY PARAMETERS: CBC, platelet count, serum glucose, chest x-ray, screening profile, coagulogram, creatinine clearance, CEA, spirometry.

END POINTS: Response/remission rate, duration of response.

CURRENT STATUS: Up to 86 patients will be entered. If no response occurs in 19 consecutively treated patients in either arm, that arm will be terminated.

DOSAGE SCHEDULE:

Arm I: DAVA - 3 mg/sqm as a slow iv push through a running iv line on days 1, 7, 15, 22, 29, and q 14 days thereafter; CACP - 120 mg/sqm or 3 mg/kg, whichever is less, by rapid iv drip with mannitol-induced diuresis and prehydration on days 1 and 29, and q 42 days thereafter; BLEO - 10 U/sqm iv loading dose on day 3, 10 U/sqm iv infusion on days 3 through 6. BLEO is repeated with the 2nd course only.

Arm II: MeGAG - 500 mg/sqm slow iv drip, repeated weekly with increments of 100 mg/sqm to maximum tolerated dose.

Patients with progressive disease after 6 weeks on either arm will be crossed over to the other arm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

7.0079 METHOTREXATE/ADRIAMYCIN/CYCLOPHOSPHAMIDE/CCNU WITH OR WITHOUT C. PARVUM OR LEVAMISOLE FOR PRIMARY LUNG CANCER

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PROTOCOL NUMBER(S) MTS-9

OBJECTIVES:

I. Determine the response rate to the combination chemotherapy with MACC: methotrexate/adriamycin/cyclophosphamide/CCNU in surgically incurable squamous cell carcinoma, adenocarcinoma, large cell anaplastic carcinoma of the lung, and other types.

II. Determine the toxicity of the chemotherapy regimen, and its modification by immunotherapy.

III. Determine whether the immunotherapy with C. parvum or LEV augments response frequency or duration when compared to same chemotherapy without immunotherapy.

IV. Study the response rates, duration of response and tolerance to the treatment according to the immune status of the patients.

V. Compare the effects of C. parvum and LEV.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with histologically or cytologically proven, measurable, surgically incurable, primary squamous cell carcinoma, adenocarcinoma or large cell anaplastic carcinoma of the lung, plus other types (undifferentiated, bronchiolar clear cell, giant cell, mucous gland, mixed adenosquamous, and small cell anaplastic carcinomas not eligible for Protocol CLB-7283. Patients must have: a performance status less than 4; life expectancy greater than 2 months; adequate hematologic, renal, and hepatic function (unless there is metastatic involvement). Patients must not have had: prior exposure to the protocol drugs; radiotherapy or surgery within 3 weeks prior to entry; hypersensitivity to horse serum, corynebacteria or their products, or thiomersal.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. MACC: Methotrexate, MTX, NSC-740; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; CCNU, NSC-79037.

Arm II: 4-Drug Combination Chemotherapy plus Immunotherapy. MACC, plus Corynebacterium parvum-Burroughs-Wellcome, C. parvum, NSC-220537.

Arm III: 4-Drug Combination Chemotherapy plus Immunotherapy. MACC, plus Levamisole, LEV, NSC-177023.

STRATIFICATION BY: Histological type.

SPECIAL STUDY PARAMETERS: SMA-6 and SMA-12; tomographies (when possible); bone survey; liver, bone, and brain scan; bone marrow aspirate and biopsy; CEA; alphafeto protein; skin tests for recall antigens; immunoglobulin levels; percent reticulocytes; in vitro lymphocyte reactions.

END POINTS: Objective tumor response, response/remission rate, duration of response, time to progression, toxicity/morbidity of treatment, immunologic competence.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: MACC: MTX - 40 mg/sqm iv (30 mg/sqm initial dose, Addendum - April 1976); ADR - 40 mg/sqm iv (total dose 550 mg/sqm) changed to 35 mg/sqm initial dose (maximum total dose 500 mg/sqm), by Addendum - April 1976; CTX - 400 mg/sqm iv; CCNU - 30 mg/sqm po. Repeat course q 3 weeks on day 1 with iv drugs in a running infusion.

Arm II: MACC; C. parvum - 3.5 mg (0.5 ml) sc (in an ordered series of 10 sites) q 7 days beginning on day 1.

Arm III: MACC as in Arm I; plus LEV - 150 mg/day po in 3 divided doses on days 1 and 2 q 7 days.

Addendum - April 1976: Hydrate patients for good urinary output. Do BUN and creatinine tests immediately prior to each treatment, and give MTX only if BUN is less than 25mg% and creatinine less than 1.5mg%. If severe stomatitis occurs, omit next dose of MTX, then escalate to 50% and 75% of dose if well tolerated.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/78

7.0080 SEQUENTIAL CMC (CTX/MTX/CCNU) AND VAP (VCR/ADR/PCB) WITH/WITHOUT RADIOTHERAPY AND WITH/WITHOUT THYMOSIN IN LIMITED LUNG CARCINOMA

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PROTOCOL NUMBER(S) NCI-78-C-19; NCI-VA-MOB-774

OBJECTIVES:

I. Determine whether addition of radiotherapy during Induction chemotherapy with CMC (cyclophosphamide/methotrexate/CCNU) followed by Maintenance chemotherapy with CMC alternating with VAP (vincristine/adriamycin/procarbazine) will increase the CR rate and prolong survival of patients with limited small cell lung cancer compared to chemotherapy alone.

II. Determine the patterns of relapse of patients treated with chemotherapy alone or with radiotherapy.

III. Determine the toxicity of radiotherapy in this treatment program.

IV. Determine whether thymosin treatment increases the response rate and prolongs survival in patients treated with chemotherapy or chemotherapy plus radiotherapy.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with histologically confirmed small cell carcinoma or mixed small cell–nonsmall cell carcinoma. Patients must be inoperable and have disease confined to one hemithorax but including bilateral mediastinal and bilateral supraclavicular nodes. Disease must be measurable or evaluable, and patients must have adequate bone marrow and renal function. Patients must be ambulatory and have a performance status of 0-2. There must be no active second malignancy or symptomatic heart disease.

PROTOCOL OUTLINE: Study randomized for Induction only.

Induction:

Arm I: 3-Drug Combination Chemotherapy plus Immunotherapy. CMC: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; CCNU, NSC-79037; plus Thymosin, no NSC number.

Arm II: 3-Drug Combination Chemotherapy plus Radiotherapy plus Immunotherapy. CMC: CTX; MTX; CCNU; plus Thymosin; plus Radiotherapy.

Arm III: 3-Drug Combination Chemotherapy. CMC: CTX; MTX; CCNU.

Arm IV: 3-Drug Combination Chemotherapy plus Radiotherapy. CMC: CTX; MTX; CCNU; plus Radiotherapy.

Maintenance: Two alternating 3-Drug Combination Chemotherapies. CMC: CTX; MTX; CCNU; alternating with VAP: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Procarbazine, PCB, NSC-77213.

STRATIFICATION BY: Morphologic subtype (small cell vs. mixed small cell and other morphology), participating institutions.

SPECIAL STUDY PARAMETERS: Chest x-ray, lung tomograms, hemogram, liver and kidney function tests, bone marrow biopsy, percutaneous liver biopsy and peritoneoscopy, fiberoptic bronchoscopy, CSF studies, liver and spleen scans, brain and bone scans, EMI and ACTA scans, metastatic bone survey, skin tests, pulmonary function tests, HLA typing and markers studies, abdominal ultrasonography.

END POINTS: Response/remission rate, duration of response, survival, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: A total entry of 80-100 patients is anticipated.

DOSAGE SCHEDULE:

Induction:

Arm I: CMC: CTX - 1500 mg/sqm iv on days 1 and 22; CCNU - 100 mg/sqm po on day 1; MTX - 15 mg/sqm po on days 1, 4, 8, 11, 22, 25, 29, and 32; plus Thymosin - 60 mg/sqm sc 3 times weekly for a total of 6 weeks.

Arm II: CMC: CTX; MTX; CCNU plus Thymosin as in Arm I plus 4000 rads in 15 fractions over 3 weeks starting within 3 days of the institution of Chemotherapy, treating the entire involved area of lung and mediastinum. All CR to receive 2000 rads of prophylactic cranial irradiation in 5 fractions over 5 days during week 13 of treatment.

Arm III: CMC: CTX; MTX; CCNU as in Arm I.

Arm IV: CMC: CTX; MTX; CCNU as in Arm I plus 4000 rads as in Arm II.

Maintenance: Begin 6 weeks after the start of Induction. VAP: VCR - 1.4 mg/sqm (maximum 2 mg) iv on days 1 and 22; ADR - 60 mg/sqm iv on days 1 and 22, total cumulative dose not to exceed 500 mg/sqm; PCB - 100 mg/sqm po on days 1 through 10 and 21 through 31. For the initial course give PCB at 50 mg on the first day, 100 mg on the second day, and the full dose (not to exceed 200 mg) on the third day and thereafter. Six weeks after the initiation of VAP begin CMC: CTX - 500 mg/sqm iv on days 1 and 22; CCNU - 50 mg/sqm po on day 1; MTX - 10 mg/sqm po on days 1, 4, 8, 11, 22, 25, 29, and 32. Thereafter alternate VAP and CMC, each course beginning 6 weeks after the initiation of the other.

Patients with no change or progression at 12 weeks go off study. If disease is still confined to the chest after restaging at progression and if the patient has not received Radiotherapy, he is eligible for Radiotherapy at that time. Patients who develop progressive disease at any time after week 12 go off study. Responding patients will be treated for 52 weeks, after which they will remain under observation only.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

7.0081 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) WSU-C-27678

OBJECTIVES:

I. Determine the antitumor effect of AMSA in advanced cancers of the lung.

II. Determine the nature and extent of toxicity of AMSA administered on an every three week schedule.

PROTOCOL ENTRY CRITERIA: Patients with measurable, biopsy-proven incurable malignancy of the lung who are not eligible for a higher priority protocol. Patients must have a minimum life expectancy of 6 weeks. They must have passed the nadir of myelosuppression from prior therapy, and radiotherapy encompassing major bone marrow sites must have been completed 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions, histological type.

SPECIAL STUDY PARAMETERS: SMA-17, Coomb's test, haptoglobin.

END POINTS: Response/remission rate, duration of response, duration of survival, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 56-100 patients will be entered.

DOSAGE SCHEDULE:

AMSA - 75 mg/sqm iv on day 1. Repeat course q 3 weeks. Doses of 40 mg/sqm and 55 mg/sqm will be used to start very poor-risk and poor-risk patients, respectively. (Poor-risk: over 65 years old, wbc between 2,000 and 4,000, platelets between 100,000 and 75,000, prior extensive radiotherapy to more than 50% of marrow bearing areas, and/or prior intolerance to chemotherapy and moderately impaired liver function; very poor-risk: patients with severely impaired liver function.) Doses will be escalated if tolerated. Evaluate after 2 courses and remove from study patients with progressive disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 11/78

7.0082 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED CANCER OF THE LUNG

Baker, L., Wayne State University, United Hospitals of Detroit, 4160 John R St., Detroit, Michigan, 48235, United States of America
PROTOCOL NUMBER(S) WSU-C-30579

OBJECTIVES:

I. Determine effect of methyl-GAG (MeGAG) on advanced cancers of the lung.

II. Determine nature and extent of toxicity of MeGAG when administered weekly.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, incurable cancer of the lung who are not eligible for higher priority protocols. Patients must have normal kidney function and an expected survival of at least 6 weeks. Patients must have passed nadir of myelosuppression from prior chemotherapy, and radiotherapy encompassing a major bone marrow site must have been completed 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Methyl-GAG, MeGAG, NSC-32946.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Performance status, tumor measurement, liver and kidney function, SMA-17.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 56 to 100 patients will be entered.

DOSAGE SCHEDULE:

MeGAG - 500 mg/sqm iv infusion over 30 min (400 mg/sqm for poor-risk patients) q weeks for 4 weeks followed by 2 weeks of rest. Increase dose by increments of 50 mg/sqm in each subsequent course to a maximum of 600 mg/sqm. Remove from study patients with disease progression (greater than 50% increase in size of lesion or appearance of new lesions) or patients with unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

7.0083 PHASE II CHEMOTHERAPY WITH PCNU FOR ADVANCED LUNG CARCINOMA

Fraile, R. J., (313-494-6433) Wayne State University, Department of Oncology, 4160 John R Street, Detroit, Michigan, 48201, United States of America
PROTOCOL NUMBER(S) WSU-C-35580

OBJECTIVES:

I. Determine the antitumor effect of PCNU in patients with advanced lung cancer.

II. Ascertain the nature and extent of toxicity of PCNU administered every 6 weeks.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven advanced lung cancer whose life expectancy is at least 6 weeks and who have clearly measurable disease. Patients must not be eligible for higher priority protocols. There must be recovery from toxicities of earlier chemotherapy, and radiotherapy to a major bone marrow site must have been completed at least 3 weeks prior to entry. Liver and kidney function must be adequate. Patients may not have had prior therapy with other nitrosoureas.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PCNU, NSC-95466.

STRATIFICATION BY: Prognostic risk (good vs. poor), histologic type (oat cell vs. squamous vs. large cell vs. adenocarcinoma).

SPECIAL STUDY PARAMETERS: Performance status, tumor measurement, chest x-ray, hemogram, renal and hepatic function studies.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 14-25 patients in each histologic subcategory will be entered.

DOSAGE SCHEDULE:

PCNU - 100 mg/sqm iv infusion over 1 hour. Initial dose for poor-risk patients is 75 mg/sqm. Repeat q 6 weeks. In the absence of toxicity, escalate to next dosage level (increase of 25 mg/sqm). Patients with progressive or unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PCNU - 50 mg vials.

DATE SUMMARIZED: 08/80

7.0084 PHASE III STUDY OF CHEMOTHERAPY WITH ADR/CCNU/HMM/MTX AND AMPHOTERICIN B IN ADVANCED LUNG CANCER

Presant, C. A., (213-359-8111) City of Hope Medical Center, Duarte, California, 91010, United States of America
PROTOCOL NUMBER(S) CA-LUN-1

OBJECTIVES:

I. Determine if amphotericin B increases response rates or survival in patients treated with chemotherapy who have non small cell bronchogenic carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with non small cell lung cancer, unresectable, no prior chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Adriamycin, ADR, NSC-123127; CCNU, NSC-79037; Hexamethylmelamine, HMM, NSC-13875; Methotrexate, MTX, NSC-740.

Arm II: Arm I plus Amphotericin B, NSC-527017.

STRATIFICATION: Performance status, histological type.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/survival.

CURRENT STATUS: 25 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: ADR - 40 mg/sqm iv days 2 and 30; CCNU - 70 mg/sqm po day 3; HMM - 40 mg/sqm po qid days 3-16 and 31-45; MTX - 10 mg/sqm po qid day 3, 10, 31 and 38.

Arm II: Arm I plus Amphotericin B - 7.5 mg/sqm day 1, 30 mg/sqm days 2 and 30.

Repeat Arm I and II sequence every 8 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; CCNU - 10, 40, 100 mg capsules; HMM - 100 mg capsules; MTX - 5 and 50 mg vials; Amphotericin B - 50 mg vials with 41 mg sodium desoxycholate and 25.2 mg sodium phosphate for iv use only.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 00250280

7.0085 BCG IMMUNOTHERAPY ADJUVANT TO RADIOTHERAPY FOR INOPERABLE BRONCHOGENIC CARCINOMA WITHOUT DISTANT METASTASES

Stefani, S. S., (312-343-7200, Ext. 2170) Veterans Administration Hines Hospital, Therapeutic Radiology Service (114B), Hines, Illinois, 60141, United States of America
PROTOCOL NUMBER(S) IL-LUN-1

OBJECTIVES:

I. Evaluate the effectiveness of immunotherapy with Tice BCG (BCG) as an adjuvant therapy to radiation therapy and as a maintenance therapy at monthly intervals vs. radiation therapy alone for bronchogenic carcinoma.

PROTOCOL ENTRY CRITERIA: Male patients with locally advanced bronchogenic carcinoma who are candidates for curative radiation therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy plus Radiotherapy. Tice BCG, BCG, NSC-116327; Radiotherapy, Co-60 irradiation.

Arm II: Radiotherapy. Co-60 irradiation.

STRATIFICATION BY: Histologic grade.

SPECIAL STUDY PARAMETERS: Immunocompetence status (skin tests for 4 recall antigens; DNCB; Total T, Active T, B cells)

END POINTS: Toxicity/morbidity of treatment, onset of distant metastases, quality and duration of survival.

CURRENT STATUS: 84 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: BCG vaccination by multiple puncture tine technique, one pre-Radiotherapy, then once a week for 12 weeks and monthly thereafter. Radiotherapy - 6,000 rads, midplane chest, in 40 days.

Arm II: Radiotherapy - 6,000 rads, midplane chest, in 40 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - vials containing 1-2 x 10 to the eighth organisms.

DATE SUMMARIZED: 04/80

7.0086 COMPARISON OF CHEST WALL AND ARM VACCINATION WITH BCG FOR BRONCHOGENIC CARCINOMA

Warren, S. E., (312-297-0520) 1600 Dempster Street, Park Ridge, Illinois, 60068, United States of America

PROTOCOL NUMBER(S) IL-LUN-3

OBJECTIVES:

I. Compare the relative effectiveness of the BCG-Tice vaccination using a site of vaccination on the chest wall and a site peripherally on the arms in modifying the survival from bronchogenic carcinoma.

PROTOCOL ENTRY CRITERIA: Patients between 18 and 80 years of age with histologically proven bronchogenic carcinoma. Patients must have a life expectancy of at least 3 months and no serious infection, active bleeding, severe systemic disease or metastatic disease to the liver or brain.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-B116327. Arm vaccination.

Arm II: Immunotherapy. BCG. Chest wall vaccination.

STRATIFICATION BY: Stage and histologic type of neoplasm.

SPECIAL STUDY PARAMETERS: Immunocompetence status tests, radiologic studies as appropriate, CBC, SMA-12, chest x-ray, tumor measurement.

END POINTS: Response/remission rate, duration of response, disease-free interval, survival rate, length of survival.

CURRENT STATUS: 65 patients have been entered as of June 1980.

DOSAGE SCHEDULE:

Arm I: BCG - 1 x 10 to the 8th CFU, percutaneously by multipuncture disc method applied to the lower anterior chest wall, weekly for 12 weeks, thereafter q 4 weeks for 9 months, thereafter q 3 months.

Arm II: BCG as in Arm I, applied to the upper portion of the right and left arm alternately, once a week for 12 weeks, thereafter q 4 weeks for 9 months, thereafter q 3 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 0.5 x 10 to the 8th CFU ampules.

DATE SUMMARIZED: 08/80

7.0087 IMMUNOTHERAPY WITH BCG FOR LUNG CANCER STAGES I THROUGH III

Kerry, R. L., (313-973-2800) St. Joseph's Mercy Hospital, P.O. Box 995, Ann Arbor, Michigan, 48106, United States of America

PROTOCOL NUMBER(S) MI-LUN-1

OBJECTIVES:

I. Determine whether immunotherapy with BCG-Tice will improve the cure rate in the three categories of lung cancer: Class A patients who are potentially cured by operation; Class B patients who have residual disease after surgery and receive radiation therapy; and Class C patients who have no surgical intervention and who receive radiation therapy.

PROTOCOL ENTRY CRITERIA: Patients with lung cancer Stages I through III.

PROTOCOL OUTLINE: Randomized study.

Patients are classified as A (prior potentially curative Surgery), B (residual disease following Surgery and undergoing Radiotherapy), and C (no Surgery and undergoing Radiotherapy). Within each classification, patients are randomized to Arm I or Arm II.

Arm I: Single-agent Immunotherapy. BCG-Tice, BCG, NSC-B116327. Isoniazid, INH, NSC-9659.

Arm II: No further treatment.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BCG - 1 ampule intrapleurally via the chest in Class A and B patients within 3 days of pneumonectomy (via thoracentesis in Class C patients); INH - 300 mg/day po for 3 weeks beginning 14 days following BCG. Five weeks after completion of Isoniazid, give systemic BCG - multipuncture tine technique to 6 sites (internal mammary, supraclavicular, and axillary areas).

Arm II: No further treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - ampules containing 2 to 8 x 10 to the eighth CFU.

Summary as provided by investigator.

DATE SUMMARIZED: 05/80

7.0088 NONSPECIFIC IMMUNOSTIMULATION WITH BCG IN TREATMENT OF BRONCHOGENIC CANCER

Neshat, A. A., Veterans Administration Medical Center, Asheville, North Carolina, 28805, United States of America

PROTOCOL NUMBER(S) NC-LUN-2

OBJECTIVES:

I. Determine the efficacy of intrapleural BCG as nonspecific immunotherapy in treatment of bronchogenic carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with Stage I and II resectable bronchogenic carcinoma.

PROTOCOL OUTLINE: Nonrandomized pilot study.

Single-agent Immunotherapy. BCG-Glaxo, BCG.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Recurrence, response, rate of survival.

CURRENT STATUS: 33 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

BCG - 1 ampule intrapleural.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 00330280

7.0089 IMMUNOTHERAPY WITH BCG FOR PRIMARY RESECTABLE NON-OAT CELL LUNG CANCER

McKneally, M. F., Albany Medical Center Hospital, Division of Cardiothoracic Surgery, 622 Medical Education Bldg., Albany, New York, 12208, United States of America

PROTOCOL NUMBER(S) NY-LUN-1

OBJECTIVES:

I. Evaluate the effect of intrapleural immunotherapy with BCG-Tice on the quality of survival and survival rate in patients with resectable lung cancer.

II. Compare the relative effectiveness of intrapleural BCG vs. intrapleural BCG followed by multiple cutaneous doses of BCG by the tine technique.

PROTOCOL ENTRY CRITERIA: Patients with resectable primary lung cancer: squamous, adeno- and anaplastic other than small (oat) cell. There must be either no detectable disease or minimal tumor burden following resection. Patients must not show postoperative cardiac instability.

PROTOCOL OUTLINE: Randomized study. Original protocol: Patients were stratified by cell type and Stage I, II, and III patients were randomized into Arms I and II. Current protocol: Patients are stratified by cell type; Stage I patients are randomized into Arms III and IV.

Arm I: Immunotherapy. Tice BCG, BCG, NSC-B116327, plus Isoniazid, INH, NSC-9659. (Closed to patient entry January 1977.)

Arm II: Control group. INH only. (Closed to patient entry January 1977.)

Arm III: Immunotherapy. BCG, intrapleural, plus INH.

Arm IV: Immunotherapy. BCG, intrapleural and cutaneous, plus INH.

STRATIFICATION BY: Stage of disease, cell type.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Length of survival.

CURRENT STATUS: Up to 116 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BCG - 1 x 10 to the seventh CFU intrapleural, 3 to 7 days after surgery. INH - 300 mg/day po for 90 days. (Arm closed to patient entry.) .

Arm II: INH - 300 mg/day po for 90 days. (Arm closed to patient entry.)

Arm III: BCG plus INH as in Arm I.

Arm IV: BCG - 1 x 10 to the seventh CFU intrapleural, 3 to 7 days after surgery; BCG - 2.5 x 10 to the eighth CFU cutaneously by tine technique at 1, 2, 3, 6, 12, 18, 24, 36, and 48 months. INH - 300 mg/day po for 90 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

7.0090 ADJUVANT IMMUNOTHERAPY WITH BCG OR BCG PLUS NEURAMINIDASE-TREATED TUMOR CELLS FOR RESECTED LUNG CANCER

Young, W. V., (216-233-7178) Sheffield Medical Park, 1511 Lincoln Blvd., East, Lorain, Ohio, 44055, United States of America

PROTOCOL NUMBER(S) OH-LUN-1

OBJECTIVES:

I. Determine whether adjuvant immunotherapy with BCG or BCG plus irradiated neuraminidase-treated autologous or homologous tumor cells can improve survival in resected lung cancer patients.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented lung cancer who have undergone resection of the primary and who do not have extrathoracic metastases.

PROTOCOL OUTLINE: Randomized study. Patients electing no further treatment enter Arm I; others are randomized to Arms II and III.

Arm I: No further treatment.

Arm II: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm III: Immunotherapy. BCG; plus irradiated, neuraminidase-treated, autologous or homologous tumor cells.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Skin testing, lymphocytotoxicity vs. cultured tumor cells, studies of serum blocking factors, measurements of leukocyte levels.

END POINTS: Interval until recurrence or metastasis, survival, immune status.

CURRENT STATUS: 149 patients have been entered as of October 1980.

DOSAGE SCHEDULE:

Arm I: No treatment.

Arms II and III: Immunotherapy to consist of id vaccination beginning 1 month postoperatively or following the completion of postoperative Radiotherapy and continuing at monthly, bimonthly, or trimonthly intervals for 2 years. Patients go off study upon the development of extrathoracic metastases.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

7.0091 ADJUVANT IMMUNOTHERAPY WITH LEVAMISOLE FOR NON-SMALL CELL LUNG CANCER

Harvey, H. A., (717-534-8677) The Milton S. Hershey Medical Center, The Pennsylvania State University, Dept. of Medicine/Div. of Oncology, Hershey, Pennsylvania, 17033, United States of America

PROTOCOL NUMBER(S) PA-MSHMC-LUN-1; JRD-12564/014C

OBJECTIVES:

I. Assess the efficacy of adjuvant immunotherapy with levamisole (LEV) in prolonging disease-free survival following 'curative' resection for lung cancer.

PROTOCOL ENTRY CRITERIA: Patients at least 18 years of age with primary lung cancer (non-small cell). Patients must have undergone resection with curative intent and have received no radiation therapy.

PROTOCOL OUTLINE: Randomized, double-blind study.

Arm I: Immunotherapy. Levamisole, LEV, NSC-177023.

Arm II: Placebo.

STRATIFICATION BY: Histology (squamous, adenocarcinoma, undifferentiated large cell); disease stage (I, II, III).

SPECIAL STUDY PARAMETERS: Skin tests for delayed hypersensitivity.

END POINTS: Relapse/recurrence rate, disease-free interval, rate and duration of survival, toxicity.

CURRENT STATUS: 30 patients had been accrued as of February 1980.

DOSAGE SCHEDULE:

Arm I: LEV - 2.5 mg/kg po on 2 consecutive days per week for 24 months.

Arm II: Placebo.

Dosage modifications for toxicity are given.

DOSAGE FORMS: LEV - 50 mg film-coated tablets; placebo tablets.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00300280

7.0092 ADJUVANT TUMOR SPECIFIC ACTIVE IMMUNOTHERAPY OF SQUAMOUS CELL CARCINOMA OF THE LUNG

Takita, H., Roswell Park Memorial Institute, Department of Thoracic Surgery, 666 Elm Street, Buffalo, New York, 14263, United States of America

PROTOCOL NUMBER(S) RPMI-PPC-445

OBJECTIVES:

I. Evaluate the efficacy of adjuvant tumor specific active immunotherapy and non-specific immunotherapy (Freund's complete adjuvant) in squamous cell carcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients who have had a curative resection (lobectomy or pneumonectomy) for Stage I or Stage II squamous cell carcinoma of the lung.

PROTOCOL OUTLINE: Randomized study.

Arm I: Control. No further treatment.

Arm II: 2-Agent Immunotherapy. Tumor-specific active Immunotherapy with solubilized tumor-associated antigen in a vehicle of Freund's complete adjuvant.

Arm III: Single-agent Immunotherapy. Freund's complete adjuvant.

STRATIFICATION BY: Stage of disease, participating institutions.

SPECIAL STUDY PARAMETERS: CEA; serial skin tests with DNCB, PPD, and tumor associated antigen.

END POINTS: Length of disease-free period, length of survival.

CURRENT STATUS: 80 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Observation and immunologic monitoring only.

Arm II: Tumor antigen of pooled allogeneic squamous cell carcinoma of the lung administered in a vehicle of Freund's complete adjuvant three times at monthly intervals beginning 14-21 days postoperatively: tumor antigen preparation - 0.500 mg; Freund's complete adjuvant - 0.3-0.5 ml.

Arm III: Freund's complete adjuvant alone, same dose and schedule as Arm II.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Does not apply.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

7.0093 SURGERY AND ADJUVANT IMMUNOTHERAPY WITH BCG AND LEVAMISOLE FOR COMPLETELY RESECTED NON-SMALL CELL CANCER OF THE LUNG

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PROTOCOL NUMBER(S) WA-LUN-1; NOG-2177

OBJECTIVES:

I. Compare potential efficacy of immunotherapy with intrapleural BCG plus levamisole placebo vs. immunotherapy with combined intrapleural BCG and levamisole vs. BCG placebo and levamisole placebo in patients following resection for non-small cell carcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven squamous cell carcinoma, adenocarcinoma, or undifferentiated large cell carcinoma of the lung. Patients with undifferentiated small cell (oat cell) carcinoma will not be included. Lung cancer must be completely resected prior to entry. Patients must have no serious concomitant disease; they must have adequate renal, pulmonary, and hepatic function.

PROTOCOL OUTLINE: Randomized, non-blind study.

All patients upon entry will be assigned to one of four strata by clinical TNM classification: Stratum I (T1N0M0); Stratum II (T2N0M0 and T1N1M0); Stratum III (T2N1M0); and Stratum IV (T3N0M0 and T3N1M0). Prior to Surgery, patients will be randomly assigned either Levamisole or Levamisole placebo. Patients in Strata I, II, III, or IV who were assigned Levamisole will receive active BCG (Arm I); patients in Strata I or II who were assigned Levamisole placebo will be randomly assigned active BCG (Arm II) or BCG placebo (Arm III).

Arm I: Surgery plus 2-Drug Immunotherapy. BCG, unspecified, no NSC number; Levamisole, LEV, NSC-177023; Isoniazid, INH, NSC-9659.

Arm II: Surgery plus Single-agent Immunotherapy. BCG; Levamisole placebo; INH.

Arm III: Control. Surgery plus BCG/INH placebo plus LEV placebo.

STRATIFICATION BY: Participating institutions; TNM classification; age: less vs. more than 60 years; cell type: squamous vs. nonsquamous; resection: total vs. subtotal pneumonectomy.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; immunologic tests.

END POINTS: Disease-free interval, recurrence rate, length of survival.

CURRENT STATUS: An accrual rate of approximately 70 patients per year in Strata I, II, and III is anticipated. Approximately three years of patient accrual will be required.

DOSAGE SCHEDULE:

Arm I: Resection of primary tumor (lobectomy when possible); LEV - 2.5 mg/kg po on days -3, -2, and -1 prior to Surgery and beginning 4-5 days postsurgery, on two consecutive days per week for 18 months; BCG - 10 to the seventh viable units ip on day 4 following Surgery; INH - 300 mg/day for 12 consecutive weeks beginning 2 weeks following BCG administration.

Arm II: Surgery as in Arm I; plus BCG as in Arm I; plus LEV/INH placebo administered in the same fashion as LEV and INH in Arm I.

Arm III: Surgery as in Arm I; BCG placebo plus LEV and INH placebo administered in the same fashion as BCG, LEV, and INH in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 1-8 x 10 to the eighth units/ampule; LEV - 50 mg tablets.

DATE SUMMARIZED: 08/80

7.0094 IMMUNOTHERAPY WITH INTRATUMORAL BCG PRIOR TO SURGERY FOR CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) YALE-L-1

OBJECTIVES:

I. Evaluate the efficacy of intratumoral immunotherapy with BCG prior to surgery in patients with carcinoma of the lung.

PROTOCOL ENTRY CRITERIA: Patients with non-small cell lung cancer who are candidates for resectional surgery and are less than age 80.

PROTOCOL OUTLINE: Prospective randomized study.

Arm I: Immunotherapy plus Surgery. Intratumoral BCG-Tice, BCG, NSC-B116327; plus Surgery.

Arm II: Surgery. Resection directly upon randomization.

STRATIFICATION BY: Clinical (Radiographic) Stage I vs. Stage II (Modified Mountain Staging).

SPECIAL STUDY PARAMETERS: Immune status.

END POINTS: Recurrence and/or death.

CURRENT STATUS: 64 patients have been entered as of June 1980.

DOSAGE SCHEDULE:

Arm I: BCG - 10 to the seventh organisms intratumoral in patients with negative PPD skin test, and 5 x 10 to the sixth organisms in patients with positive PPD skin test. Surgery for both groups 14-21 days later. Isoniazid - 300 mg/day for 12 weeks, beginning 14 days after intratumoral BCG, to prevent overgrowth of BCG organisms.

Arm II: Surgery. Isoniazid - as in Arm I, as control factor.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - vials containing 5 x 10 to the eighth colony-forming units.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 00640680

7.0095 ADJUVANT IMMUNOTHERAPY WITH FREUND'S COMPLETE ADJUVANT (FCA) OR FCA/TUMOR ANTIGEN FOR BRONCHOGENIC CARCINOMA

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PROTOCOL NUMBER(S) CAN-NCIC-BR2

OBJECTIVES:

I. Evaluate the ability of a program of immunotherapy to extend the disease free interval and prolong survival in a large group of lung cancer patients with minimal residual tumor mass who are, however, at high-risk, that is, those who have had a 'definitive' surgical procedure but about whom it is known that there will be a recognized high-risk of recurrent disease in a fixed postsurgical period of time.

II. Determine whether the addition of specific tumor antigen Freund's complete adjuvant (FCA) confers immunotherapeutic benefit beyond that which might be achieved with FCA alone.

III. Compare patients receiving one or the other of these therapies to a third group of concurrently randomized patients who will receive no treatment.

IV. Assess the effect of the treatment program on various parameters of both in vitro and in vivo immune function. Obtain information through immunological monitoring and through ancillary investigations done in a number of participating institutions.

PROTOCOL ENTRY CRITERIA: Patients with Stage I or II epidermoid large cell or adenocarcinoma of the bronchus, or Stage I small cell anaplastic carcinoma. Patients must have no detectable residual tumor after surgery and no evidence of metastases. Patients must not have had prior postoperative Chemotherapy nor active tuberculosis or antituberculosis therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. Freund's Complete Adjuvant (FCA). Mycobacterium hominis, Difco brand.

Arm II: Immunotherapy. FCA homogenized with lung tumor antigen (LTA) - histopathological type similar to patients disease.

Arm III: No therapy.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum protein electrophoresis, LDH, liver, brain and bone scans, in vitro lymphocyte function, serum complement, cell mediated immunity, skin tests for recall antigens.

END POINTS: Disease free interval, survival rate, immunocompetence.

CURRENT STATUS: 300 patients will be entered in 1 1/2 years.

DOSAGE SCHEDULE: Begin Immunotherapy 10 to 30 days following surgery. Give all injections on the same side as the operation, the first and third in the deltoid region, the second into the anterior thigh. Therapy for progressive disease is at the discretion of the investigator.

Arm I: FCA - 0.3 ml intradermal (id) q month for 3 months.

Arm II: FCA - 0.3 ml and 500 microgram LTA in 0.3 ml saline id q month for 3 months.

Arm III: No therapy.

Follow all patients at least 5 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: LTA - 500 microgram syringes; FCA - Difco - 10 mg syringes.

DATE SUMMARIZED: 11/78

7.0096 COMBINATION CHEMOTHERAPY WITH VCR/ADR/CTX/CACP/CCNU VS ADR/CTX/CACP FOR ADVANCED BRONCHOGENIC CANCERS

Kleiman, S., Instituto Fundacion Arturo Lopez Perez, Hospital del Salvador, Rancagua 878, Santiago, Chile
PROTOCOL NUMBER(S) CHILE-LUN-1

OBJECTIVES:

I. Measure the effectiveness of vincristine (VCR)/adriamycin (ADR)/cyclophosphamide (CTX)/cis-platinum (CACP)/CCNU and ADR/CTX/CACP in the treatment of advanced bronchogenic cancer.

II. Determine the toxicity of both combinations.

III. Determine the influence of treatment on survival by comparing responsive and nonresponsive groups.

PROTOCOL ENTRY CRITERIA: Patients with evaluable histologically or cytologically proven bronchogenic cancer of known histologic type that is not amenable to surgery. Patients must be no more than 70 years of age and must have adequate renal, cardiac, and bone marrow function and a Karnofsky-Zubrod performance status of 3 or less. There must have been no prior therapy with any of the protocol agents.

PROTOCOL OUTLINE: Randomized study.

Arm I: 5-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; cis-Platinum, CACP, NSC-119875; CCNU, NSC-79037.

Arm II: 3-Drug Combination Chemotherapy. ADR; CTX; CACP.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Respiratory function; bronchofibroscopy; hepatic, bone, and brain scans.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, survival time, duration of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: VCR - 1.4 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 2; CTX - 500 mg/sqm iv on day 2; CACP - 20 mg/sqm iv (micro drops over 30 minutes) on days 1 through 5. Repeat q 21 days. CCNU - 60 mg/sqm po. Repeat q 6 weeks. Continue therapy until relapse.

Arm II: ADR - 60 mg/sqm iv on day 1; CTX - 600 mg/sqm iv on day 1; CACP - 60 mg/sqm iv infusion over 6 hours on day 1. Repeat q 21 days until relapse.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/80

7.0097 RADIOTHERAPY ALONE OR WITH CTX/MTX/CCNU CHEMOTHERAPY AND/OR BCG IMMUNOTHERAPY FOR LUNG CANCER

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PROTOCOL NUMBER(S) EORTC-08742; ITA-MIL-7307

OBJECTIVES:

I. Evaluate the effect on survival in patients treated by radiotherapy alone and compare these patients with those receiving additional treatment.

II. Evaluate the addition of chemotherapy with cyclophosphamide (CTX), methotrexate (MTX) and CCNU in patients responding to prior radiotherapy.

III. Evaluate the addition of nonspecific immunostimulation with BCG in patients responding to prior radiotherapy, its effect on the patients' delayed hypersensitivity reactions as demonstrated by skin tests, and compare the benefits of this immunotherapy with those obtained by chemotherapy.

IV. Evaluate the addition of multimodal therapy: chemotherapy as in II plus immunotherapy as in III on patients who have responded to prior radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients with regional epidermoid bronchopulmonary cancer without clinically detectable metastases who are not eligible for surgery and have had no prior radiotherapy, immunotherapy or chemotherapy. Patients may have had an exploratory thoractomy 2 to 4 weeks previously and may have homolateral supraclavicular adenopathy. Patients must have adequate hematological function and performance status equal to or better than 40 (Karnofsky) and must be considered good risks after initial evaluation.

PROTOCOL OUTLINE: Enter all patients to Regimen A, then randomize patients who respond with complete or incomplete (better than 50%) tumor regression to Arms I, II, III, or IV.

Regimen A: Radiotherapy. Cobalt-60, betatron or linear accelerator to the tumor, the mediastinal nodes and to the involved supraclavicular areas as necessary.

Arm I: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; CCNU, NSC-79037.

Arm II: Immunotherapy. BCG Pasteur, BCG, NSC-B116328.

Arm III: 3-Drug Combination Chemotherapy plus Immunotherapy. CTX, MTX, CCNU plus BCG.

Arm IV: No further therapy.

STRATIFICATION BY: Participating institutions, prior exploratory thoractomy.

SPECIAL STUDY PARAMETERS: Skin tests: tuberculin, Candida, CCB Pasteur; fiberoptic bronchoscopy.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, appearance of metastases.

CURRENT STATUS: 400 patients will be entered. 235 patients have been entered as of March 1980.

DOSAGE SCHEDULE:

Regimen A: 5000-6000 rads given over a period of 5 to 6.5 weeks to the primary tumor, 4500 rads to the mediastinum and 5000-6000 rads to the involved supraclavicular fossae. Evaluate patients at the completion of Radiotherapy, if possible, by fiberoptic bronchoscopy and biopsy. Remove from study patients with disease progression or without change and follow for life. Randomize complete and partial responders to Arms I, II, III, or IV.

Enter patients within 15 days of completion of Radiotherapy.

Arm I: Repeat course q 4 weeks for 12 months. CTX - 1 gram/sqm iv or im; MTX - 40 mg/sqm iv or im; CCNU - 70 mg/sqm po.

Arm II: Repeat course q 4 weeks for 18 months. BCG - 0.2 ml (concentration not given) id in each of 4 sites.

Arm III: CTX/MTX/CCNU, as in Arm I, plus BCG, as in Arm II.

Continue Chemotherapy and/or Immunotherapy as long as indicated or until prior local or distant metastases occur.

Arm IV: No further therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CCNU - 40 and 100 mg capsules; others not given.

DATE SUMMARIZED: 01/77

PATIENT ACCRUAL: 02350380

7.0098 RADIOTHERAPY PLUS CHEMOTHERAPY WITH CTX, VCR, MECCNU, BLEO, ADR, MTX, PLUS HMM FOR UNDIFFERENTIATED BRONCHOGENIC CARCINOMA

Levy, P., (Villejuif 677.24.69) European Org. for Research on Treatment of Cancer, Bronchial Carcinoma Cooperative Group, Unite de Recherches Statistiques, Inst. Gustave Roussy, 16B Paul Vaillant Couturier, 94800 Villejuif, France

PROTOCOL NUMBER(S) EORTC-08743

OBJECTIVES:

I. Compare Consolidation therapies in patients with limited (regionally confined) disease: induce remission in these patients with radiotherapy combined with cyclophosphamide(CTX)/vincristine (VCR) chemotherapy, then randomize responders to continued CTX/VCR therapy vs. Consolidation with COMB: CTX/VCR/methyl-CCNU (MeCCNU)/bleomycin(BLEO).

II. Compare COMB vs. COM: CTX/VCR/MeCCNU - with and without prophylactic brain irradiation in patients with extensive disease.

III. Evaluate the efficacy of adriamycin(ADR) plus methotrexate (MTX) for patients in relapse following the initial therapy.

IV. Evaluate the efficacy of hexamethylmelamine(HMM) for patients in relapse following ADR plus MTX therapy.

PROTOCOL ENTRY CRITERIA: Patients with measurable disease parameters of limited or extensive disease of undifferentiated - oat cell or mixed cell type - carcinoma of the lung. Extensive disease is defined as affecting both lungs, both supraclavicular areas or presenting with distant metastases. Patients must have an expected survival time of more than 2 months, a performance status of 40 or better (Karnofsky), and they must have adequate hematological and renal functions. They may not have had prior radiotherapy, chemotherapy or surgery, except biopsy.

PROTOCOL OUTLINE: Enter patients with limited disease to Regimen A, and those with extensive disease to Regimen B.

Regimen A: All patients enter Induction. Patients in complete remission or good partial remission (better than 50% tumor regression) following Induction are randomized for Consolidation.

Induction: Radiotherapy plus 2-Drug Combination Chemotherapy. Cobalt-60, betatron or linear accelerator plus Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574.

Consolidation:

Arm I: 2-Drug Combination Chemotherapy. CTX; VCR; as in Induction.

Arm II: 4-Drug Combination Chemotherapy. COMB: CTX; VCR; Methyl-CCNU, MeCCNU, NSC-95441; Bleomycin, BLEO, NSC-125066.

Regimen B: Patients with extensive disease are randomized to Arms III, IV, V, and VI.

Arm III: 4-Drug Combination Chemotherapy. COMB: CTX; VCR; MeCCNU; BLEO.

Arm IV: 3-Drug Combination Chemotherapy. COM: CTX; VCR; MeCCNU.

Arm V: 4-Drug Combination Chemotherapy plus Radiotherapy. COMB as in Arm III plus prophylactic brain irradiation.

Arm VI: 3-Drug Combination Chemotherapy plus Radiotherapy. COM: CTX; VCR; MeCCNU plus prophylactic brain irradiation.

Failures from Regimen A Consolidation (patients in relapse or with progressive disease other than brain metastases) and patients who fail to respond to Regimen B Arm III, IV, V, or VI enter Regimen C. Failures on Regimen C proceed to Regimen D. Patients on Regimen A Consolidation with signs of brain metastases as the only symptom of disease progression receive additional Radiotherapy on Regimen E. Patients with painful brain metastases may receive palliative Radiotherapy.

Regimen C: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740.

Regimen D: Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

Regimen E: Radiotherapy. Irradiation of the brain.

STRATIFICATION BY: Participating institutions, extent of disease.

SPECIAL STUDY PARAMETERS: Liver scan followed by laparoscopy with liver biopsies, brain scan, skin tests: tuberculin-Pasteur, Candida, vaccine CCB-Pasteur.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response.

CURRENT STATUS: 80-100 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Regimen A:

Induction: Radiotherapy: Enter patients 10-14 days following diagnostic thoracotomy if this was performed. 4500 rads given over a period of 4 to 5 weeks to the primary tumor, the mediastinum and, in the presence of adenopathy, to the homolateral supraclavicular region, plus Chemotherapy: CTX - 1.2 mg/sqm iv q 3 weeks beginning on the evening of day 1 of Radiotherapy; VCR - 1.5 mg/sqm iv q 3 weeks on days 1 and 8. If no disease progression is observed, repeat entire course once for a total of 2 courses. Remove from protocol all patients with disease progression or with less than 50% tumor regression 2 weeks after completion of Induction therapy. Randomize responders for Consolidation therapy.

Consolidation:

Arm I: CTX, VCR, as in Arm I, q 3 weeks until relapse or disease progression.

Arm II: CTX - 600 mg/sqm iv on day 1 q 4 weeks; MeCCNU - 80 mg/sqm po on day 1 q 4 weeks; VCR - 0.75 mg/sqm iv on day 2 q 7 days for 20 weeks; BLEO - 10 mg/sqm iv given 6 hours after VCR on day 2 q 7 days for 20 weeks.

Regimen B:

Arm III: CTX - 800 mg/sqm iv on day 1 q 4 weeks; MeCCNU - 100 mg/sqm po on day 1 q 4-6 weeks; VCR - 1.5 mg/sqm iv on day 2 q 7 days for 20 weeks; BLEO - 20 mg/sqm iv given 6 hours after VCR on day 2 q 7 days for 20 weeks.

Arm IV: CTX, MeCCNU, VCR as in Arm III.

Arm V: Radiotherapy to the entire brain plus CTX; MeCCNU; VCR; BLEO as in Arm III.

Arm VI: Radiotherapy to the entire brain plus CTX; MeCCNU; VCR as in Arm III.

Regimen C: ADR - 45 mg/sqm iv single dose q 3 weeks; MTX - 40 mg/sqm iv single dose q 3 weeks. When relapse or disease progression occurs, enter patients to Regimen D.

Regimen D: HMM - 150 mg/sqm/day po until further relapse.

Regimen E: 3000 rads given over a period of 2 to 3 weeks to the entire brain with or without corticosteroids or diuretics given concomitantly with Consolidation Therapy.

Palliative Radiotherapy (1500 to 3000 rads) may be given for painful brain metastases.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules; MeCCNU - 50 and 100 mg capsules; HMM - 50 and 100 mg capsules; MTX - 50 mg ampules; CTX - 100, 200 and 500 mg ampules; BLEO - 15 mg vials; VCR - 1 mg ampules.

DATE SUMMARIZED: 01/77

7.0099 CHEMOTHERAPY WITH CTX VS CTX/DEHYDROEMETINE FOR EVALUABLE CARCINOMA OF THE LUNG

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PROTOCOL NUMBER(S) EORTC-73009

OBJECTIVES:

I. Compare the response-remission rate and duration of response in patients with inoperable primary carcinoma of the lung treated with cyclophosphamide with and without dehydroemetine.

PROTOCOL ENTRY CRITERIA: Patients with inoperable, evaluable primary carcinoma of the lung.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm II: 2-Drug Combination Chemotherapy. CTX; Dehydroemetine, NSC-131546.

STRATIFICATION BY: Histological type: epidermoid, adenocarcinoma, and other.

SPECIAL STUDY PARAMETERS: Electrocardiogram; tuberculin skin test; Candida skin test; mumps skin tests; CCB skin test; liver and brain scans.

END POINTS: Response/remission rate, disease-free interval, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 40 patients will be entered.

DOSAGE SCHEDULE:

Arm I: CTX - 1.1 mg/sqm iv q 3 weeks.

Arm II: CTX - 1.1 mg/sqm iv q 3 weeks; Dehydroemetine - 3.5 mg/kg im once a week.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100 and 200 mg capsules; Dehydroemetine - 20 and 60 mg ampules.

DATE SUMMARIZED: 02/77

7.0100 IMMUNOTHERAPY WITH MYCOBACTERIUM SMEGMATIS ATCC 607 AS ADJUVANT THERAPY TO SURGERY IN PRIMARY BRONCHOGENIC CARCINOMA

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PROTOCOL NUMBER(S) FRE-PAR-CPB-0177

OBJECTIVES:

I. Determine whether immunotherapy with M. smegmatis ATCC 607, when added to surgery, improves survival of patients who have undergone full resection of primary lung carcinoma.

PROTOCOL ENTRY CRITERIA: Patients of both sexes and all ages who have resectable, potentially curable lung carcinoma and are candidates for surgery. All histologic types, oat cell anaplasic carcinoma excepted.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery.

Arm II: Surgery plus Immunotherapy. Mycobacterium smegmatis ATCC 607.

STRATIFICATION BY: TNM classification.

SPECIAL STUDY PARAMETERS: Immunocompetence status, skin tests for recall antigens, DNCB.

END POINTS: Morbidity of treatment, response/remission rate, disease-free interval.

CURRENT STATUS: 300 patients will be entered; 200 have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: Lung resection; lobectomy or pneumonectomy; full resection.

Arm II: Lung resection as in Arm I, plus post-operative Immunotherapy beginning 30 days after operation. Subcutaneous injection of heat-killed M. smegmatis in suspension of 2 mg bacilli per 1 ml distilled water. Monthly injections of 0.2 ml of bacilli suspension at 4 sites. Duration of treatment: at least 2 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: M. smegmatis - 2 mg vials.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 02000280

7.0101 ADJUVANT THERAPY WITH VP-16213 VS PLACEBO FOR NON-OAT CELL BRONCHOGENIC CARCINOMA

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PROTOCOL NUMBER(S) ITA-MIL-LC791

OBJECTIVES:

I. Check the utility of prolonged, continual medical surveillance as regards collateral pathology, and prompt diagnosis of local and/or systemic recurrences.

II. Check the efficacy of chemotherapy with VP-16213 in comparison with a control group.

III. Check the course of the immunological status between treated and placebo groups.

IV. Check the role in survival of prognostic factors: sex, age, presurgical symptoms, type of surgery, weight loss.

PROTOCOL ENTRY CRITERIA: Patients with Stage I and II non-oat cell bronchogenic carcinoma after surgery which left no residual disease. Patients must have had no previous chemotherapy with antiblastic agents.

PROTOCOL OUTLINE: Randomized, double-blind study.

Arm I: Single-agent Chemotherapy. VP-16213, VP-16, NSC-141540.

Arm II: Placebo.

STRATIFICATION: Participating institutions, disease stage, immunologic status.

SPECIAL STUDY PARAMETERS: Bronchoscopy, immunologic status.

END POINTS: Response/remission rate, survival rate, survival time, toxicity/morbidity of treatment, duration of response, quality of survival, time to recurrence or metastases.

CURRENT STATUS: Patients will be accepted over a period of 24 months.

DOSAGE SCHEDULE:

Arm I: VP-16 - 500 mg/sqm po divided over days 1 to 3. Repeat course q 28 days if toxicity permits for 12 months or until disease progresses.

Arm II: Placebo - given in the same manner as VP-16 in Arm I.

Discontinue therapy if unacceptable hematologic toxicity develops. Follow all patients q 6 months in the first 2 years, then q year for a total of 5 years or until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VP-16 - 100 mg vials.

DATE SUMMARIZED: 11/79

7.0102 COMBINATION CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE (CTX)/HEXAMETHYLMELAMINE (HMM) VS CTX/VP-16213 FOR INOPERABLE NON-OAT CELL LUNG CANCER

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PROTOCOL NUMBER(S) ITA-MIL-LC792

OBJECTIVES:

I. Compare the efficacy of the combinations cyclophosphamide (CTX)/VP-16213 (VP-16) vs. CTX/hexamethylmelamine (HMM) in the treatment of inoperable lung cancer and in resected lung cancer with residual disease.

II. Assess the efficacy of the combination of CTX/HMM in the 2nd stage after additional therapy with VP-16 in operated no residual disease patients who have recurrences.

III. Assess the quality of life in patients with inoperable lung cancer and in operated patients with residual disease who have undergone antiblastic therapy.

PROTOCOL ENTRY CRITERIA: Patients with limited inoperable histologically proven non-oat cell lung cancer (T1T2T3N1N2Mo) or locally recurring disease after surgery which left no residual disease. Patients must have a performance status over 50 and have no previous radiotherapy nor any chemotherapy other than VP-16.

PROTOCOL OUTLINE: Randomized study: Enter patients with recurrent disease from Protocol ITA-MIL-LC791 directly to Arm I. Randomize all other patients to Arms I and II.

Arm I: Induction and Maintenance:

2-Drug Combination and Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Hexamethylmelamine, HMM, NSC-13875.

Arm II: Induction and Maintenance:

2-Drug Combination Chemotherapy. CTX; VP-16213, VP-16, NSC-141540.

STRATIFICATION: Participating institutions, prior therapy.

SPECIAL STUDY PARAMETERS: Bronchoscopy, immunologic status.

END POINTS: Response/remission rate, duration of response, survival rate, quality of life, objective tumor response.

CURRENT STATUS: Patients will be entered over a period of 24 months.

DOSAGE SCHEDULE:

Arm I: Induction: Enter patients with residual disease within 15 days of surgery, all others within 1 week of randomization. CTX - 1000 mg/sqm iv on day 1; HMM - 100 mg/sqm po on days 1 through 14. Repeat course q 21 days for 3 months. Enter patients with stable or responsive disease to maintenance, remove all others from study.

Maintenance: CTX - 1000 mg/sqm iv on day 1: HMM - 100 mg/sqm po on days 1 through 4. Repeat course q 2 months for 9 months.

Arm II: Induction: CTX as in Arm I; VP-16 - 500 mg/sqm po on days 1 through 3. Repeat course q 21 days for a total of 4 courses. Enter patients with stable or responsive disease to maintenance, remove all others from study.

Maintenance: CTX as in Arm I; VP-16 - 500 mg/sqm po on days 1 through 3.

Repeat course q 2 months for 9 months.

Remove from study all patients with disease progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

7.0103 CHEMOTHERAPY WITH CTX PLUS LONG-TERM VS SHORT-TERM BCG IMMUNOTHERAPY ADJUVANT TO SURGERY IN STAGE I LUNG CANCER

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PROTOCOL NUMBER(S) JAP-NCCH-L-1

OBJECTIVES:

I. Confirm that long-term BCG administration can further improve survival of patients with Stage I lung cancer compared with short-term BCG, based on the positive data of an earlier protocol study.

PROTOCOL ENTRY CRITERIA: Patients with Stage I lung cancer, as evaluated by surgicopathological examination.

PROTOCOL OUTLINE: Randomized study.

Arm I: Short-term Immunotherapy plus Single-agent Chemotherapy plus Surgery. BCG, Japan BCG Institute, BCG; plus Cyclophosphamide, CTX, NSC-26271.

Arm II: Long-term Immunotherapy plus Single-agent Chemotherapy plus Surgery. CTX as in Arm I; plus BCG.

STRATIFICATION BY: Stage of lung cancer.

SPECIAL STUDY PARAMETERS: Skin test.

END POINTS: Survival.

CURRENT STATUS: 52 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: BCG - dosage not specified, given one week before surgery, tine technique, then 4 times serially once a month after Surgery; CTX - 1 mg/kg po daily after surgery for an extended period.

Arm II: CTX as in Arm I; BCG as in Arm I, then every 3 months as long as possible.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 00520280

SECTION 8

LYMPHOMA

8A. HODGKIN'S DISEASE

CCG-541 PHASE III EXTENDED VS INVOLVED FIELD RADIOTHERAPY WITH OR WITHOUT MOPP CHEMOTHERAPY FOR CHILDHOOD HODGKIN'S DISEASE 8.0001
CLB-7451 PHASE III STUDY OF RADIOTHERAPY AND CHEMOTHERAPY WITH VCR/PCB/BCNU/PRED AND CLB FOR STAGE III HODGKIN'S DISEASE 8.0002
CLB-7551 COMBINATION CHEMOTHERAPY WITH CCNU/VBL/PCB/PRED AND CHLORAMBUCIL AND RADIOTHERAPY FOR ADVANCED HODGKIN'S DISEASE 8.0003
CLB-7552 CCNU/VBL/PCB/PRED OR BLEO/ADR/VCR/SZC & CHLORAMBUCIL AND IMMUNOTHERAPY WITH MER-BCG FOR HODGKIN'S DISEASE STAGES IIIB AND IV 8.0004
CLB-7751 CVPP (CCNU/VBL/PCB/PRED) ALONE OR IN COMBINATION WITH INVOLVED OR EXTENDED FIELD RADIOTHERAPY FOR HODGKIN'S DISEASE 8.0005
EST-1476R RADIOTHERAPY VS ADR/BLEO/VBL/DTIC CHEMOTHERAPY AS CONSOLIDATION FOLLOWING BLEO-MOPP INDUCTION FOR ADVANCED HODGKIN'S DISEASE 8.0006
SEG-75HD0103 PHASE III CHEMOTHERAPY WITH BCNU/CTX/VBL/PCB/PRED/BLEO ALTERNATING WITH ADR/DTIC/BLEO FOR HODGKIN'S DISEASE 8.0007
SEG-77HD0103 PHASE III CHEMOTHERAPY WITH BCNU/CTX/VBL/PCB/PRED WITH OR WITHOUT RADIOTHERAPY FOR HODGKIN'S DISEASE 8.0008
SWOG-7612 RADIOTHERAPY AND CHEMOTHERAPY WITH MOPP-BLEO (NM/VCR/BLEO/PCB/PRED) VS A-COPP (ADR/CTX/VCR/PRED/PCB) FOR STAGE III HODGKIN'S DISEASE IN CHILDREN 8.0009
SWOG-7808 CHEMOTHERAPY WITH MOP-BAP PLUS IMMUNOTHERAPY WITH LEV AND INVOLVED FIELD RADIOTHERAPY FOR STAGES III AND IV HODGKIN'S DISEASE 8.0010
SWOG-7903/7961 CHOP CHEMOTHERAPY FOR PATIENTS WITH HODGKIN'S DISEASE - MOPP FAILURES, STAGES III OR IV (7903) OR PREVIOUSLY UNTREATED (7961) 8.0011
BCRP-7808 ALTERNATING MOPP (NM/VCR/PCB/PRED) AND SCAB (SZC/CCNU/ADR/BLEO) VS MOPP ALONE FOR ADVANCED HODGKIN'S DISEASE 8.0012
BCRP-7824 RADIOTHERAPY AND CHEMOTHERAPY WITH MOPP (NM/VCR/PCB/PRED) ALONE OR COMBINED FOR EARLY HODGKIN'S DISEASE 8.0013
MDAR-176 CHEMOTHERAPY AND HORMONE THERAPY WITH ADR/DTIC/BLEO/CCNU/PRED (ABDIC) FOR HODGKIN'S DISEASE REFRACTORY TO CONVENTIONAL THERAPY 8.0014
MDAR-37 COMBINATION CHEMOTHERAPY AND HORMONE THERAPY WITH NM/CTX/PCB/PRED PLUS RADIOTHERAPY FOR GENERALIZED HODGKIN'S DISEASE 8.0015
UICC-76118 RADIOTHERAPY ALONE OR WITH COMBINATION CHEMOTHERAPY WITH MOPP (NM/VCR/PCB/PRED) FOR HODGKIN'S DISEASE STAGES I AND II 8.0016

UICC-77016 CHEMOTHERAPY WITH MOPP (NM/VCR/PCB/PRED) WITH LIMITED OR EXTENDED RADIOTHERAPY FOR HODGKIN'S DISEASE 8.0017

8B. NON-HODGKIN'S LYMPHOMA AND OTHER SPECIFIED LYMPHOMAS

CCG-551 PHASE III STUDY OF RADIOTHERAPY PLUS CHEMOTHERAPY WITH COMP VS MODIFIED LSA2-L2 FOR NON-HODGKIN'S LYMPHOMA IN CHILDREN 8.0018

CLB-7851 PHASE III INDUCTION WITH COPA VS COPA/BLEO & CONSOLIDATION WITH HIGH DOSE MTX/CF VS MTX FOR DIFFUSE HISTIOCYTIC AND LYMPHOCYTIC LYMPHOMA 8.0019

CLB-7902 PILOT CHEMOTHERAPY WITH MTX/VM-26/PCB/DM FOR REFRACTORY, POOR HISTOLOGY OR NODULAR, POORLY DIFFERENTIATED LYMPHOCYTIC LYMPHOMA 8.0020

CLB-7951 PHASE III CHEMOTHERAPY WITH CTX VS CTX/ADR/VCR/BLEO/PRED FOR STAGES III AND IV NODULAR POORLY DIFFERENTIATED LYMPHOCYTIC LYMPHOMA 8.0021

EST-4477 PHASE III CTX/PRED INDUCTION AND CONSOLIDATION VS RADIOTHERAPY CONSOLIDATION FOR STAGE III OR IV NODULAR NON-HODGKIN'S LYMPHOMA 8.0022

EST-5477 PHASE III COPA VS COPA & BLEO VS CAP-BOP & RADIOTHERAPY CONSOLIDATION FOR UNFAVORABLE HISTOLOGIC SUBTYPES OF NON-HODGKIN'S LYMPHOMA 8.0023

SEG-77NHL0103 PHASE III CHEMOTHERAPY WITH BCOP (BCNU/CTX/VCR/PRED) VS CHOP (CTX/ADR/VCR/PRED) FOR NON-HODGKIN'S LYMPHOMA 8.0024

SWOG-7433 PHASE III STUDY OF RADIOTHERAPY WITH OR WITHOUT CHOP (CTX/ADR/VCR/PRED) CHEMOTHERAPY FOR NON-HODGKIN'S LYMPHOMA 8.0025

SWOG-7713/14 PHASE III COP VS CHOP CHEMOTHERAPY PLUS LEV & BCG IMMUNOTHERAPY & LEV MAINTENANCE FOR STAGES III & IV NON-HODGKIN'S LYMPHOMA .. 8.0026

SWOG-7905 PHASE III INDUCTION WITH ACOP, CNS THERAPY, & MAINTENANCE WITH ACOP/6-MP/MTX (IV & IT)/HC FOR CHILDHOOD NON-HODGKIN'S LYMPHOMA ... 8.0027

BCRP-7312A PHASE III CHEMOTHERAPY WITH CAVP (CTX/ADR/VCR/PRED) VS CVP (CTX/VCR/PRED) FOR DISSEMINATED NON-HODGKIN'S LYMPHOMA 8.0028

MDA-3 COMBINATION RADIOTHERAPY, CHEMOTHERAPY AND IMMUNOTHERAPY FOR STAGE III NON-HODGKIN'S LYMPHOMA 8.0029

MDAR-215 CHOP PLUS LATE INTENSIFICATION WITH COAP-BLEO, AND ALTERNATE THERAPIES FOR NONRESPONDING PATIENTS WITH NON-HODGKIN'S LYMPHOMA 8.0030

MDAR-260 CHEMOTHERAPY WITH CHOP-BLEO PLUS MAINTENANCE WITH OAP IN PEPA PROGRAM FOR DIFFUSE HISTIOCYTIC LYMPHOMA 8.0031

MDAR-288 PHASE II CHEMOTHERAPY WITH AMSA FOR NON-HODGKIN'S LYMPHOMA 8.0032

MDAR-5 RADIOTHERAPY, CHEMOTHERAPY WITH CHOP-BLEO, AND IMMUNOTHERAPY FOR STAGE III NON-HODGKIN'S LYMPHOMA 8.0033

MDAR-84 RADIOTHERAPY, CHEMOTHERAPY WITH CTX/ADR/VCR/BLEO, HORMONE THERAPY WITH PRED, & BCG IMMUNOTHERAPY FOR STAGES I & II NON-HODGKIN'S LYMPHOMA 8.0034

MSKCC-7676 COMBINATION THERAPY WITH THIO-TEPA/VCR/CLB/PRED/RADIOTHERAPY PLUS CTX/ADR/L-PAM/PRED WITH/WITHOUT MBV IMMUNOTHERAPY FOR NON-HODGKIN'S LYMPHOMA 8.0035

MSKCC-7920 CHOP (CTX/ADR/VCR/PRED) VS BLEO-CHOP CHEMOTHERAPY FOR ADVANCED STAGES OF DIFFUSE B-CELL LYMPHOMA 8.0036

NCI-77-C-145 CHOP (CTX/ADR/VCR/PRED) PLUS MTX PLUS IT MTX AND ARA-C WITH OR WITHOUT INITIAL SURGERY FOR CHILDHOOD NON-HODGKIN'S LYMPHOMA 8.0037

NCI-78-C-145 OBSERVATION VS INTENSIVE CHEMOTHERAPY FOR NODULAR LYMPHOMAS AND DIFFUSE WELL-DIFFERENTIATED LYMPHOCYTIC LYMPHOMAS 8.0038

SJCRH-NHL-78-I/II COMBINATION CHEMOTHERAPY WITH PRED, CTX, VCR, MTX, AND 6-MP PLUS RADIOTHERAPY FOR STAGE I-II NON-HODGKIN'S LYMPHOMA IN CHILDREN 8.0039

ARG-GATLA-1-LRS-79 PHASE III INDUCTION SINGLE-AGENT CHEMOTHERAPY CTX VS COMBINATION CTX/VCR/PRED WITHOUT MAINTENANCE IN NON-HODGKIN'S LYMPHOMA 8.0040

ARG-GATLA-7701 CHEMOTHERAPY WITH BACOP (BLEO/ADR/CTX/VCR/PRED) VS COPP (CTX/VCR/PCB/PRED) FOR ADVANCED DIFFUSE HISTIOCYTIC LYMPHOMA 8.0041

CAN-UICC-76002 BCG IMMUNOTHERAPY FOR DIFFUSE NON-HODGKIN'S LYMPHOMA BEING TREATED BY RADIOTHERAPY AND C-MOPP CHEMOTHERAPY 8.0042

COSTA-RICA-L278 CHEMOTHERAPY WITH CTX, VCR, PRED, MTX, 6-MP, AND ADR WITH AND WITHOUT SURGERY FOR PEDIATRIC NON-HODGKIN'S LYMPHOMA 8.0043

POL-NHL-1 PHASE II TOTAL BODY IRRADIATION FOR STAGE III AND IV NON-HODGKIN'S LYMPHOMA 8.0044

SAFR-CT-LEU/LYM-A RADIOTHERAPY WITH OR WITHOUT CHEMOTHERAPY WITH ADR/VP-16, CMM/VP-16, OR CMM FOR LYMPHOCYTIC LYMPHOMA 8.0045

SAFR-CT-LEU/LYM-C CHEMOTHERAPY WITH VP-16/ADR VS CHOP (CTX/ADR/VCR/PRED) VS VP-16/CMM FOR LARGE CELL LYMPHOCYTIC LYMPHOMA 8.0046

8C. LYMPHOMA—GENERAL

CLB-7972 PHASE II CHEMOTHERAPY WITH AMSA FOR REFRACTORY HODGKIN'S AND DIFFUSE HISTIOCYTIC OR LYMPHOCYTIC LYMPHOMA 8.0047

EST-1480 PHASE II SINGLE-AGENT CHEMOTHERAPY WITH N-(PHOSPHONOACETYL)-L-ASPARTATE OR AMSA FOR PREVIOUSLY TREATED LYMPHOMA 8.0048

SWOG-7912 PHASE II STUDY OF GALLIUM NITRATE FOR HODGKIN'S AND NON-HODGKIN'S LYMPHOMA 8.0049

SWOG-7918 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED HODGKIN'S AND NON-HODGKIN'S LYMPHOMA 8.0050

SWOG-7967 PHASE II PILOT CHEMOTHERAPY WITH DAVA/BCNU/ADR/PRED FOR REFRACTORY HODGKIN'S AND NON-HODGKIN'S LYMPHOMA 8.0051

SWOG-8005 PHASE II PILOT CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE FOR REFRACTORY MALIGNANT LYMPHOMA 8.0052

BCRP-8005 PHASE II CHEMOTHERAPY WITH SPIROGERMANIUM FOR REFRACTORY LYMPHOMA 8.0053

MDAR-406 SEQUENTIAL CHEMOTHERAPY WITH IMVP-16 (IPP/MTX/VP-16), HOP (ADR/VCR/PRED), OR OAP-BLEO (ARA-C/BLEO/PRED/VCR) FOR STAGE IV LARGE CELL LYMPHOMA 8.0054

MSKCC-8081 PHASE II COMBINATION CHEMOTHERAPY WITH METHYL-GAG/VM-26 FOR ADVANCED MALIGNANT LYMPHOMA 8.0055

NCI-78-C-34 CHEMOTHERAPY FOR STAGE III/IV DIFFUSE LYMPHOMAS WITH PROMACE (CTX/ADR/VP-16/PRED/MTX) AND MOPP (NM/VCR/PCB/PRED) 8.0056

NCI-79-C-93 TBI PLUS CHEMOTHERAPY WITH ARA-C/CTX PLUS AUTOLOGOUS BONE MARROW THERAPY FOR RECURRENT LYMPHOMA 8.0057

SECTION 8

LYMPHOMA

8A. HODGKIN'S DISEASE

8.0001 PHASE III EXTENDED VS INVOLVED FIELD RADIOTHERAPY WITH OR WITHOUT MOPP CHEMOTHERAPY FOR CHILDHOOD HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) CCG-541; SWOG-7660

OBJECTIVES:

I. Compare the effectiveness of involved field radiotherapy followed by MOPP chemotherapy, and extended field radiotherapy, in treating laparotomy-confirmed Stage I and II Hodgkin's disease in children in terms of:

(A) Duration of disease-free interval following completion of initial therapy.

(B) The type and extent of disease following initial therapy.

(C) Survival.

II. Determine the retrievability of new disease following primary therapy for each of the three regimens, using specified retrieval plans.

III. Determine the effect of specific histology on results of primary and retrieval therapy for each of the three regimens.

IV. Determine the comparative effects of the three treatment regimens with respect to:

(A) Linear growth, bi-acromial and bi-cristal diameters.

(B) Incidence of hypothyroidism and sterility.

(C) Incidence of second malignancies.

(D) Complications following staging celiotomy and splenectomy, immediate and remote, including fulminating infections.

(E) Effectiveness of penicillin prophylaxis in the prevention of post-splenectomy infectious complications.

PROTOCOL ENTRY CRITERIA: Patients under 18 years of age with histologically confirmed Stage I and II untreated Hodgkin's disease. Patients who have undergone either prior chemotherapy or radiotherapy are excluded except for patients with massive mediastinal disease who required local radiotherapy for tumor shrinkage. Patients with Stage I unilateral upper neck disease of any histology other than lymphocytic depletion; patients with Stage I unilateral inguinal disease of any histology are excluded from randomization but are to be registered and followed on therapy as prescribed by their Principal Investigator.

PROTOCOL OUTLINE: Randomized study. Randomize SWOG patients to Arm I, II or IV only, all other patients to Arms II or III only.

Arm I: Involved Field Radiotherapy.

Arm II: Involved Field Radiotherapy. 3-Drug Combination Chemotherapy plus Hormone Therapy. MOPP: Nitrogen mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023, for CCG and CLB patients.

Arm III: Extended Field Radiotherapy.

Arm IV: No further therapy.

STRATIFICATION BY: Stage and class of disease, primary disease site, participating institutions.

SPECIAL STUDY PARAMETERS: X-ray and flat plate of abdomen, SMA 12/60, serum copper, Hb isozymes of alkaline phosphatase, sedimentation rate. Tests on specific indication - PTH, EKG, cardiac sonography, lymphangiogram, bone marrow and liver biopsy. T3, T4 and TSH at 6 and 12 months after completion of therapy and yearly thereafter (Addendum 1, April 1979). Optional tests - quarterly test of immunocompetence FSH, on completion of therapy and yearly thereafter (Addendum 1, April 1979).

END POINTS: Response/remission rate, toxicity/moribidty of treatment, survival rate, duration of survival, objective tumor response, duration of disease-free interval, type and extent of disease extensions, local recurrence and progression.

CURRENT STATUS: 150 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Involved Field Radiotherapy (IF) - Supervoltage of at least 2 MeV or Cobalt 60 capable of covering the area described at the 80% margin - Orthovoltage and Cesium units are contraindicated. Involved regions are treated to a total basic midplane tumor dose of 3500-4000 rads at a rate of 850-1000 rads tumor dose once a week. Additional or booster treatment may be given for residual disease for a total of 500-1000 rads if normal tissue tolerance is not exceeded. At first relapse, randomize to IF and adjuvant chemotherapy, MOPP, as in Arm II.

Arm II: Involved Field Radiotherapy as in Arm I plus Adjuvant Chemotherapy, MOPP, beginning 4 weeks following completion of IF radiotherapy. NM - 6 mg/sqm iv on days and 8 q course; VCR - 1.4 mg/sqm iv (top dose 2 mg) on days 1 and 8; PCB - 100 mg/sqm/day po divided into 2 or 3 doses on days 2 through 14; PRED - 40 mg/sqm/day po divided into 3 doses on days 1 through 14 on initial and fourth courses only, after 28 days, repeat for 6 courses. At first relapse, repeat involved field radiotherapy plus give 6 more courses of MOPP.

Arm III: Extended Field Radiotherapy - total dose of 3500 rads divided into 20 fractions in 4 weeks at age 11 or above and also ages 6 through 10 and total doses of 2500 rads divided into 20 fractions in 4 weeks at ages 5 or under. At first relapse, repeat EF and give 6 courses of MOPP.

Arm IV: No further therapy. (Enter SWOG patients only).

Dosage modifications for toxicity are given as indicated by Hb, wbc and platelet.

DOSAGE FORMS: VCR - 1 mg and 5 mg vials; NM - 10 mg vials; PCB - 50 mg capsules; PRED - 5 mg tablets.

DATE SUMMARIZED: 05/79

PATIENT ACCRUAL: 01370279

8.0002 PHASE III STUDY OF RADIOTHERAPY AND CHEMOTHERAPY WITH VCR/PCB/BCNU/PRED AND CLB FOR STAGE III HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) CLB-7451

OBJECTIVES:

I. Compare long-term, multiple-agent chemotherapy either alone or in combination with total nodal radiotherapy with total nodal radiation therapy alone.

II. Compare tolerance of patients to these treatments of various intensities.

III. Compare the quality of response, duration of response, and survival rates of the therapeutic groups.

IV. Compare tolerance of therapy for patients with and without prior splenectomy for staging.

V. Study patterns to relapse in the various study groups.

PROTOCOL ENTRY CRITERIA: Patients under 65 years of age with Stage III Hodgkin's disease (by Ann Arbor Conference criteria), who are previously untreated or have received regional radiotherapy with no recurrence in the treatment area. (Patients must have biopsy-proven Stage IIIA disease; those with Stage IIIB disease should be entered on Pilot Study 7903 or Study 7551. Addendum 4, November 1979.)

PROTOCOL OUTLINE: Randomized study.

Arm I: Induction: Total nodal Radiotherapy.

Arm II: Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574. Procarbazine, PCB, NSC-77213. BCNU, NSC-409962. Prednisone, PRED, NSC-10023.

Maintenance: Single-agent Chemotherapy. Chlorambucil, CLB, NSC-3088. (Use of Chlorambucil as Maintenance therapy in this protocol has been discontinued, as per Addendum 3, September 1978.)

Arm III: Induction: Total nodal Radiotherapy, 3-Drug Combination Chemotherapy plus Hormone Therapy.

Arm IV: Induction: 3-Drug Combination Chemotherapy plus total nodal Radiotherapy. (Arm IV is closed to patient entry, as per Addendum 2, July 1978.)

STRATIFICATION BY: Participating institutions, symptom classification, disease staging, prior surgery (laparotomy).

SPECIAL STUDY PARAMETERS: Radiological assessment of tumor size, tomograms, spleen scan, IV pyelogram, laparotomy or needle biopsy of liver, lower extremity lymphogram, precise clinical and pathological staging.

END POINTS: Response/remission rate, duration of response, quality of response, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 200 patients will be entered in 2.5 years.

DOSAGE SCHEDULE:

Arm I: Induction: Total nodal radiotherapy of all lymph node areas from the tips of the mastoid to the femoral triangles by the 3-and 2-field technique in 5 sequential courses given over 10 weeks. Five weeks later, give 2000 rads over 8 days to each of 3 fields sequentially as follows: field 1 - head and neck areas extending to diaphragm, field 2 - para-aortic area, spleen and, optionally, the porta hepatis, and field 3 - lymph node areas including iliac regions, pelvis and groin. Bulky disease defined as nodal areas measuring more than 5 cm in diameter may optionally receive booster doses for a total of 4500 rads. Following rest interval of 3-4 weeks, give 1800 to 2000 rads to each of 2 fields including a mantle and an inverted Y which together cover the same areas irradiated in the 3 field course. Follow up all patients q 3 months until relapse.

Arm II: Induction: VCR - 1.4 mg/sqm iv on days 1 and 7 (maximum single dose - 2 mg.); PCB - 50 mg/sqm po on day 1, 100 mg/sqm po on days 2 through 14; BCNU - 80 mg/sqm iv on day 1; PRED - 40 mg/sqm/day po on days 1 through 14. Rest two weeks, then repeat 2-week course plus rest interval 2 additional times omitting PRED. Then repeat entire 12-week sequence of courses.

Maintenance: CLB - 6 mg/sqm/day po. Begin 2 weeks after completion of Induction therapy. Continue for 3 years or until relapse.

Arm III: Induction: Arm I fractionation schedule for total nodal radiotherapy. Following 6 to 8 weeks rest, give combination chemotherapy as in Arm II, Induction only.

Arm IV: Induction: Combination chemotherapy as in Arm II. Following 2 weeks rest, given total nodal radiotherapy as in Arm I. Omit Arm II Maintenance chemotherapy.

Evaluate all patients in Arms I through IV at 6 weeks. If disease has become resistant or has progressed to stage IV, remove patients from study. Follow up all patients q 3 months until relapse. Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg ampules; others not given.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 01861078

8.0003 COMBINATION CHEMOTHERAPY WITH CCNU/VBL/PCB/PRED AND CHLORAMBUCIL AND RADIOTHERAPY FOR ADVANCED HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) CLB-7551

OBJECTIVES:

I. Compare the response rates and remission durations observed with 6 or 12 monthly cycles of chemotherapy.

II. Determine the effectiveness of a combined approach by radiotherapy and multiple-drug chemotherapy in the control of stage IV Hodgkin's disease as compared to multiple-drug chemotherapy alone.

III. Explore whether early reduction of bulk disease by radiotherapy is beneficial in controlling the disease.

IV. Explore the ability of radiotherapy to eradicate residual microscopic disease in patients with apparent complete remission after a full course of multiple-drug chemotherapy.

V. Explore the ability of radiotherapy to eradicate disease in patients with apparent partial remission after a full course of multiple-drug chemotherapy.

PROTOCOL ENTRY CRITERIA: Hodgkin's disease, Stage IV (modified Rye classification). (Patients with Stage IIIB or IV Hodgkin's disease, Luke's classification. Addendum 3, October 1979.) Patients must be previously untreated and must have measurable disease.

PROTOCOL OUTLINE: Randomized study. Following Induction, enter all responders to Maintenance.

Induction:

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. CCNU, NSC-79037; Vinblastine, VBL, NSC-49842; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023. Short-term Chemotherapy.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. Arm I Chemotherapy plus PRED. Long-term Chemotherapy.

Arm III: 3-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. CCNU; VBL; PCB; plus PRED; plus Radiotherapy. Long-term Chemotherapy.

Arm IV: 3-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. CCNU; VBL; PCB; plus PRED; plus Radiotherapy. Short-term Chemotherapy before and after Radiotherapy.

Maintenance: Single-Agent Chemotherapy. Chlorambucil, CLB, NSC-3088. (Use of Chlorambucil as Maintenance therapy has been discontinued, as per Addendum 2, September 1978.)

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Isotope scans (if necessary), serum protein electrophoresis, electrocardiogram.

END POINTS: Response rate, duration of response, duration of survival, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: About 200 patients to be entered within 2 years.

DOSAGE SCHEDULE:

Induction:

Arm I: Give 2 weeks of chemotherapy followed by 2 weeks of rest for a total of six 4-week courses. CCNU - 75 mg/sqm po on day 1; VBL - 4 mg/sqm iv on days 1 and 8; PCB - 100 mg/sqm po on days 1 through 14; PRED - 40 mg/sqm po on days 1 through 14 during the first and fourth courses only.

Arm II: CCNU, VBL, PCB, PRED as in Arm I q 4 weeks x 12 courses. Give PRED in courses 1, 4, 7 and 10 only.

Arm III: CCNU, VBL, PCB, PRED as in Arm I q 4 weeks x 6 courses, followed by radiotherapy - megavoltage: 2500 rads to all areas of gross disease known to exist prior to start of chemotherapy. Begin radiotherapy 10 weeks following the last dose of chemotherapy or following a return of wbc to more than 4000 after the 6th course of chemotherapy, whichever occurs later.

Arm IV: CCNU, VBL, PCB, PRED as in Arm I q 4 weeks x 3 courses followed by radiotherapy, as in Arm III. Four weeks after the completion of radiotherapy, give 3 more courses of Arm I chemotherapy with CCNU, VBL, PCB, PRED.

Maintenance:

Arm V: Four weeks after completion of Induction therapy give all partial or complete responders CLB - 6 mg/sqm/day po. Continue Maintenance for 3 years or until disease progression. (Use of CLB discontinued as per Addendum 2, September 1978.)

Dosage modifications for toxicity are given.

DOSAGE FORMS: CCNU - 40 and 100 mg capsules; VBL - 10 mg vials; PCB - 50 mg capsules; PRED - 50 mg tablets; CLB - 2 mg tablets.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 01881078

8.0004 CCNU/VBL/PCB/PRED OR BLEO/ADR/VCR/SZC & CHLORAMBUCIL AND IMMUNOTHERAPY WITH MER-BCG FOR HODGKIN'S DISEASE STAGES IIIB AND IV

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PROTOCOL NUMBER(S) CLB-7552

OBJECTIVES:

I. Compare remission rates and the remission duration of two 4-Drug Chemotherapy regimens employing completely different agents in previously treated patients with stage IV Hodgkin's disease.

II. Compare the response rates and remission durations of the repetitive use of the 4-Drug Combination regimens with alternative cycles of the two entirely different regimens, thus exposing the patient to eight drugs.

III. Compare the efficacy of chemotherapy and chemoimmunotherapy with respect to response rates, remission durations, and toxicity.

IV. Assess delayed MER-BCG hypersensitivity as a prognostic indicator, and compare the effects of different chemotherapies and of immunotherapy upon the delayed hypersensitivity reaction.

PROTOCOL ENTRY CRITERIA: Hodgkin's disease, stages IIIB and IV, previously treated by radiotherapy or chemotherapy. Patients must have measurable disease.

PROTOCOL OUTLINE: Randomized study. (MER Immunotherapy discontinued, closing Arms II, IV, VI and VII; Addendum 6, February 1979).

Induction:

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. CVPP: CCNU, NSC-79037; Vinblastine, VBL, NSC-49842; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy plus Immunotherapy. MER, Arm I, plus MER-BCG, CVPP, as in NSC-143769.

Arm III: 4-Drug Combination Chemotherapy. BAVS: Bleomycin, BLEO, NSC-125066; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Streptozotocin, SZC, NSC-85998.

Arm IV: 4-Drug Combination Chemotherapy plus Immunotherapy. BAVS, as in Arm III, plus MER.

Arm V: 4-Drug Combination Chemotherapy alternating with another 4-Drug Combination Chemotherapy. Arm I chemotherapy courses alternating with Arm III chemotherapy courses.

Arm VI: Alternating chemotherapy courses, as in Arm V, plus MER Immunotherapy, as in Arm II.

Maintenance: Enter all patients who have achieved partial or complete remission status after 12 courses of Induction therapy.

Arm VII: Single-agent Chemotherapy with or without Immunotherapy. Chlorambucil, CLB, NSC-3088. (Use of Chlorambucil as Maintenance therapy in this protocol has been discontinued, as per Addendum 5, September 1978). Patients who have received Immunotherapy during Induction will receive MER q 3 months.

STRATIFICATION BY: Participating institutions, sex, prior therapy, disease stage.

SPECIAL STUDY PARAMETERS: ECG, isotope scans (if necessary), serum immunoelectrophoresis, skin tests (PPD, mumps, dermatophytin, Varidase).

END POINTS: Response/remission rate, duration of remission, duration of survival, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction:

Arm I: Administer 2 weeks of chemotherapy followed by 2 weeks of rest for a total of 12 4-week courses. CCNU - 75 mg/sqm po on day 1; VBL - 4 mg/sqm iv on days 1 and 8; PCB - 100 mg/sqm/day po on days 1 through 14 (in the first course only, give 50 mg/sqm po on day 1, 75 mg/sqm po on day 2 and 100 mg/sqm po on days 3 through 14); PRED - 40 mg/sqm/day po on days 1 through 14 in courses 1, 4, 7 and 10 only.

Arm II: CCNU, VBL, PCB, PRED as in Arm I plus MER - 200 mcg iv in each of 5 sites on day 1 of each 4-week course.

Arm III: Administer 2 weeks of chemotherapy followed by 2 weeks of rest for a total of 12 4-week courses. BLEO - 5 units/sqm iv on days 1 and 8; ADR - 50 mg/sqm iv on day 1 (maximum total dose - 550 mg/sqm); VCR - 1.4 mg/sqm iv on days 1 and 8 for 6 courses (maximum dose - 2.0 mg), then 1.0 mg/sqm iv on days 1 and 8 for courses 7 through 12; SZC -1500 mg/sqm iv on days 1 and 8.

Arm IV: BLEO, ADR, VCR, SZC as in Arm III, plus MER, as in Arm II.

Arm V: Alternate Arm I chemotherapy using CCNU, VBL, PCB, and PRED given during courses 1, 3, 5, 7, 9 and 11 with Arm III chemotherapy using BLEO, ADR, VCR and SZC in courses 2, 4, 6, 8, 10, and 12.

Arm VI: Arm V, alternating combination chemotherapy, plus immunotherapy with MER, as in Arm II.

Maintenance:

Arm VII: Enter responders from Induction Arms. Beginning 21 days after the second vinca alkaloid injection of the 12th Induction course, give: CLB - 6 mg/sqm day po. In addition, give patients who received Induction therapy Arm II, IV or VI: MER - 1 mg dose as in Arm II, q 3 months, beginning 3 months after the last immunotherapy dose. Skin test all patients q 4 months. Continue Maintenance therapy until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CCNU - 40 mg, 100 mg capsules; VCR - 1 mg, 5 mg vials; PCB - 50 mg capsules; PRED - 5 mg tablets; ADR - 10 mg vials; BLEO - 15 unit ampules; VBL - 10 mg vials; SZC - 2.0 mg ampules; CLB - 2 mg tablets; and MER - 1 and 2 mg/ml vials.

DATE SUMMARIZED: 05/79

PATIENT ACCRUAL: 01781078

8.0005 CVPP (CCNU/VBL/PCB/PRED) ALONE OR IN COMBINATION WITH INVOLVED OR EXTENDED FIELD RADIOTHERAPY FOR HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) CLB-7751

OBJECTIVES:

I. Compare the efficacy of combination chemotherapy with CVPP: CCNU, vinblastine (VBL), prednisone (PRED) and procarbazine (PCB) alone, preceded by involved field radiotherapy, or preceded by extended field radiotherapy for poor risk patients with Hodgkin's disease, Stages I and II. (Extended field radiotherapy plus chemotherapy deleted, Addendum 2, February 1979.)

II. Determine whether extended field radiotherapy plus 6 cycles of CVPP prolongs the total duration of remission compared to involved field radiotherapy plus 6 cycles of CVPP or combination chemotherapy alone in poor prognosis patients. (Objective deleted, Addendum 2).

III. Determine whether combination chemotherapy alone or involved field radiotherapy plus chemotherapy significantly decreases the morbidity and/or mortality compared to extended field radiotherapy and chemotherapy.

IV. Determine the relapse patterns of disease, whether in nodal or extranodal sites, inside or outside of the irradiated fields, for each treatment program.

V. Test the influence of the three treatments upon overall survival.

VI. Document the psychologic impact and response of the patient to knowledge of relapse of disease (Addendum 1, July 1978).

PROTOCOL ENTRY CRITERIA: Patients over 16 years of age with biopsy and laparotomy-proven Stage I or II Hodgkin's disease. Patients must be in symptom class B or have mixed cellularity or lymphocyte-depleted Hodgkin's disease, and must be previously untreated by Radiotherapy or Chemotherapy. (Patients 40 years or older or patients with a mediastinal mass may be entered regardless of symptom class or histology, Addendum 2.)

PROTOCOL OUTLINE: Randomized study. Separately randomize Stage IA or IIA patients with mixed cellularity and lymphocyte depletion vs. Stage IB or IIB regardless of cell type.

Arm I: Involved Field Radiotherapy plus 3-Drug Combination Chemotherapy plus Hormone Therapy. CCNU, NSC-79037; Vinblastine, VBL, NSC-49892; Procarbazine, PCB, NSC-77213; plus Prednisone, PRED, NSC-10023. 4-Drug Combination Chemotherapy for relapse: Bleomycin, BLEO, NSC-125066; Adriamycin, ADR, NSC-123127; Streptozotocin, SZC, NSC-85998; Vincristine, VCR, NSC-67574.

Arm II: Extended Field Radiotherapy, 3-Drug Combination Chemotherapy plus Hormone Therapy. CCNU, VBL, PCB, PRED, as in Arm I. 4-Drug Combination Chemotherapy for relapse. BLEO, ADR, SZC, VCR, as in Arm I. (Arm closed, Addendum 2.)

Arm III: 3-Drug Combination Chemotherapy plus Hormone Therapy. CCNU, VBL, PCB, PRED as in Arm I. Relapse Therapy; Involved Field Radiotherapy plus 4-Drug Combination Chemotherapy for relapse. BLEO, ADR, SZC, VCR as in Arm I.

STRATIFICATION BY: Participating institutions, disease stage: IA or IIA vs. IB or IIB (all cell types, Addendum 2).

SPECIAL STUDY PARAMETERS: Liver and renal function tests, serum protein electrophoresis, pulmonary function tests, thyroid function tests, EKG, chest x-ray, evaluation of psychosocial function, laparotomy, splenectomy, liver biopsy, bone marrow biopsy, psychologic assessment (Addendum #1, July 1978).

END POINTS: Response/remission rate, survival rate, toxicity/morbidity of treatment, duration of remission, survival time, relapse patterns, incidence of second primary (corrected to incidence of acute leukemia, Addendum 2).

CURRENT STATUS: About 300 (corrected to 200, Addendum 2) patients will be entered in 3-3.5 years.

DOSAGE SCHEDULE:

Arm I: Involved Field Radiotherapy - 3500-4000 rad in 4 weeks to be delivered at 150-200 rads/day. A 500 rad boost to bulky disease is permissible. Following a 4 week rest period, initiate Chemotherapy if wbc is above 4,000, platelets above 100,000. Give 6 cycles, each 2 week cycle to be followed by a 2 week rest period: CCNU - 75 mg/sqm po on day 1; VBL - 4.0 mg/sqm iv, on days 1 and 8; PCB - 100 mg/sqm po on days 1 through 14; PRED - 40 mg/sqm po on days 1 through 14 in cycles 1 and 4 only. Combination Chemotherapy for relapse: For relapse limited to nodal areas on the same side of the diaphragm as the initial site of disease, extranodal areas, any previously irradiated node, or in hilar or mediastinal nodes, give Chemotherapy for a maximum of 12 cycles, each 2 week cycle to be followed by a 2 week rest period: BLEO - 5.0 units/sqm iv on days 1 and 8; ADR - 50 mg/sqm iv on day 1; the total dose of ADR is not to exceed 550 mg/sqm, therefore ADR should be omitted from the 12th cycle if a 12th cycle is necessary. SCZ - 1500 mg/sqm iv on days 1 and 8; VCR - Cycles 1-6: 1.4 mg/sqm iv on days 1 and 8; Cycles 7-12: 1.0 mg/sqm iv on days 1 and 8 (maximum dose of 1.5 mg). If relapse occurs in periaortic nodes which were not previously irradiated, or in nodal areas on the opposite side of the diaphragm from the initial site of disease, involved field Radiotherapy as described above will be administered, followed 4-6 weeks later with BLEO, ADR, SCZ and VCR as described above.

Arm II: Extended field Radiotherapy dosage as in Arm I. Following a 4 week rest period, Combination Chemotherapy with CVPP as in Arm I. For relapse: Combination Chemotherapy for relapse with BLEO, ADR, SCZ and VCR, as in Arm I. (Arm closed, Addendum 2.)

Remove patients in Arm I and II from study if complete remission is not achieved after 6 cycles of Chemotherapy.

Arm III: Combination Chemotherapy with CVPP as in Arm I. Remove from study patients not achieving complete remission after 9 cycles. Relapse Therapy: Involved field Radiotherapy as in Arm I, then in 4-6 weeks, Combination Chemotherapy for relapse with BLEO, ADR, SCZ and VCR as in Arm I.

Give patients in all Arms who are in complete remission after 6 courses of Chemotherapy 2 additional courses, then observe. Document the psychologic impact and response of the patient undergoing a relapse (Addendum I, July 1978).

Dosage modifications for toxicity are given.

DOSAGE FORMS: CCNU - 10, 40 and 100 mg capsules; PCB - 50 mg capsules; PRED - 5, 20 and 50 mg tablets; VBL - 10 mg vials; BLEO - 15 unit ampules; ADR - 10 mg vials; VCR - 1 and 5 mg vials; SCZ - 2 mg ampules.

DATE SUMMARIZED: 05/79

PATIENT ACCRUAL: 00091078

8.0006 RADIOTHERAPY VS ADR/BLEO/VBL/DTIC CHEMOTHERAPY AS CONSOLIDATION FOLLOWING BLEO-MOPP INDUCTION FOR ADVANCED HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) EST-1476R

OBJECTIVES:

I. Determine the incidence of CR and PR with an Induction regimen of low-dose bleomycin and MOPP (nitrogen mustard/vincristine/procarbazine/prednisone) for Hodgkin's disease of Stages IIISB, IIIB, IIISEB, IIIEB, IVA, and IVB.

II. Compare non-cross-resistant Consolidation chemotherapy using ABVD (adriamycin/bleomycin/velban/DTIC) with low-dose radiotherapy to areas of pretreatment involvement in terms of increasing the percentage of CR and of prolonging the disease-free interval in CR.

III. Determine the toxicity of Induction and Consolidation chemotherapy, especially with respect to long-term pulmonary complications of low-dose bleomycin and recovery of spermatogenesis.

IV. Determine the ease of administration and toxicity of low-dose radiotherapy after 6 cycles of intensive combination chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Hodgkin's disease of Stages IIISB, IIIB, IIISEB, IIIEB, IVA or IVB who have one measurable disease parameter. Patients must have undergone bipedal lymphangiography and bone marrow biopsy. Patients may not have had prior chemotherapy, although prior local or regional radiotherapy is allowed provided the site of relapse has not been irradiated. Patients must be between the ages of 15 and 70 years, must have adequate renal function, and must have a WBC of at least 4000 and platelets of at least 100,000.

PROTOCOL OUTLINE: Study randomized for Consolidation only.

Induction: Enter all patients.

5-Drug Combination Chemotherapy and Hormone Therapy. BLEO-MOPP: Bleomycin, BLEO, NSC-125066; Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023.

Consolidation: Randomize PR and CR from Induction to Arms I and II after stratification by CR vs. PR, over 35 years vs. under 35 years, and eligibility for radiotherapy.

Arm I: Radiotherapy. Standard megavoltage techniques.

Arm II: 4-Drug Combination Chemotherapy. ABVD: Adriamycin, ADR, NSC-123127; BLEO; Velban, VBL, NSC-49842; DTIC, NSC-45388.

STRATIFICATION BY: Participating institutions, age (over 35 vs. under 35), performance status (0-1 vs. 2-4), disease stage.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematological parameters, liver and kidney function tests, chest x-ray, lymphangiogram, abdominal flat plate, isotope and CAT scans, pulmonary function tests, and sperm count.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival

CURRENT STATUS: At the current rate of accrual, it is expected that about 360 patients will be entered over the 6 years of the study

DOSAGE SCHEDULE:

Induction:

BLEO-MOPP: Bleo - 2 mg/sqm iv on days 1 and 8; NM - 6 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm iv on days 1 and 8, maximum dose not to exceed 2 mg; PCB - 100 mg/sqm/day po for 14 days; PRED - 40 mg/sqm/day po for 14 days, every fourth cycle only. Cycle repeated q 28 days. Induction therapy is terminated if progressive disease is present after 3 cycles or if no change occurs after 6 cycles. PR and CR at 1 month after completion of 6 cycles of BLEO-MOPP are randomized to Arms I and II of Consolidation.

Consolidation:

Arm I: Begin Radiotherapy 1 month after completion of Induction Chemotherapy if WBC and platelets are at least 4000 and 100,000, respectively. Standard megavoltage techniques are used to irradiate all sites of pretreatment involvement. If sites both above and below the diaphragm are treated, therapy is given in divided courses with a rest of 2-4 weeks after the first course. The mid-plane total dose will be 1500-2000 rads at 150-200 rads/fraction, 5 times weekly. Specific site doses are: nodal sites, 2000 rads; bony sites, 2000 rads; organ sites, 1500 rads at 150 rads/day. Whole lung irradiation is delivered to 1500 rads if noncontiguous pulmonary parenchymal lesions are present.

Arm II: ABVD: ADR - 25 mg/sqm iv on days 1 and 15; BLEO - 2 mg/sqm iv on days 1 and 15; VBL - 6 mg/sqm iv on days 1 and 15; DTIC - 250 mg/sqm iv on days 1 and 15. Repeat cycles q 35 days.

Patients who are in CR 1 month after the completion of Consolidation Chemotherapy will be observed without further therapy until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; PRED - 5 and 20 mg scored tablets; BLEO - 15 unit ampules; ADR - 10 and 50 mg vials; VBL - 10 mg vials; PCB - 50 mg capsules; NM - 10 mg vials; DTIC - 100 and 200 mg vials.

DATE SUMMARIZED: 07/80

8.0007 PHASE III CHEMOTHERAPY WITH BCNU/CTX/VBL/PCB/PRED/BLEO ALTERNATING WITH ADR/DTIC/BLEO FOR HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) SEG-75HD0103; SEG-366; SEG-75HD301

OBJECTIVES:

I. Compare the response rate of BCNU, cyclophosphamide, vinblastine, procarbazine and prednisone (BCVPP) plus bleomycin given for 6 cycles with the same regimen (BCVPP) alternating with adriamycin, dacarbazine and bleomycin for 6 cycles.

II. Determine whether patients who have achieved less than complete remission on BCVPP plus bleomycin alone can subsequently respond to a regimen including adriamycin and dacarbazine.

PROTOCOL ENTRY CRITERIA: Patients with a biopsy diagnosis of Stage IIIB or IV Hodgkin's disease defined clinically using the criteria established at Ann Arbor or as discovered at laparotomy.

PROTOCOL OUTLINE: Randomized study.

Arm I. 5-Drug Combination Chemotherapy and Hormone Therapy during odd months plus 3-Drug Combination Chemotherapy during even months. BCNU, NSC-409962; Vinblastine, VBL, NSC-49842; Cyclophosphamide, CTX, NSC-26271; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023; Bleomycin, BLEO, NSC-125066 alternating with Adriamycin, ADR, NSC-123127; Dacarbazine, DTIC, NSC-45388; BLEO.

Arm II: 5-Drug Combination Chemotherapy and Hormone Therapy. BCNU; VBL; CTX; PCB; PRED; BLEO.

STRATIFICATION BY: Participating institutions; prior therapy: minimal or none.

SPECIAL STUDY PARAMETERS: Chest x-ray, lymphangiogram, biopsy or laparotomy, skin tests.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response.

CURRENT STATUS: About 334 patients will be entered.

DOSAGE SCHEDULE:

Arm I. BCNU - 100 mg/sqm, iv, on day 1; VBL - 5 mg/sqm, iv, on day 1; CTX - 600 mg/sqm, iv, on day 1; PCB - 50 mg, po, on day 1, 100 mg on day 2 and 100 mg/sqm on days 3 through 10; PRED - 60 mg/sqm, po, on days 1 through 10; and BLEO - 2 mg/sqm, iv, on days 1 and 8 during the 1st, 3rd and 5th months; alternating with ADR - 50 mg/sqm, iv, on day 1; DTIC - 625 mg/sqm, iv, on days 1 and 8; and BLEO - 2 mg/sqm, iv, on days 1 and 8 during the 2nd, 4th and 6th months.

Arm II: BCNU - 100 mg/sqm, iv, on day 1; VBL - 5 mg/sqm, iv, on day 1; CTX - 600 mg/sqm, iv, on day 1; PCB - 50 mg, po, on day 1, 100 mg on day 2 and 100 mg/sqm for days 3 through 10; PRED - 60 mg/sqm, po, for days 1 through 10; BLEO - 2 mg/sqm, iv, on day 1 and 8. Repeat cycle q 28 days for a total of 6 cycles.

Patients who have achieved less than complete remission on Arm I go off study. Cross over patients in Arm II who have achieved less than complete remission to Arm I even month therapy for at least 3 courses beyond the time that complete remission is achieved in the crossover therapy. (Addendum, September 1977). Place patients who achieve complete remission but have had prior radiotherapy, on the best Consolidation regimen achieved on SEG #340, and follow until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 11 mg vials; CTX - 100, 200, 500 mg vials and 50 mg tablets; VBL - 10 mg ampules; PCB - 50 mg capsules; PRED - 5 and 50 mg tablets; BLEO - 15 unit bottles; DTIC - 100 and 200 mg vials; ADR - 10 mg vials.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 01570878

8.0008 PHASE III CHEMOTHERAPY WITH BCNU/CTX/VBL/PCB/PRED WITH OR WITHOUT RADIOTHERAPY FOR HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) SEG-77HD0103; SEG-77HD320

OBJECTIVES:

I. Compare the disease-free survival and total survival in patients with early stage Hodgkin's disease, who have unfavorable prognostic factors, receiving either involved field radiation (IF) plus combination chemotherapy with BVCPP: BCNU, cyclophasphamide (CTX), vinblastine (VBL), procarbazine (PCB) and prednisone (PRED) or combination chemotherapy alone.

II. Determine whether IF radiotherapy will convert a partial response to chemotherapy to a complete response.

PROTOCOL ENTRY CRITERIA: Patients with Hodgkin's disease, Stages IA, B or E; IIA, B, or E and IIIA or E. Patients must be previously untreated and must have any of the following unfavorable prognostic features: age greater than 40 years, fever or weight loss over 10%, extranodal involvement, or histological diagnosis of mixed cellularity and lymphocyte depletion. Patients must have undergone a staging laparotomy. Protocol open to all patients with mediastinal mass.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus 4-Drug Combination Chemotherapy plus Hormone Therapy. BVCPP: BCNU, NSC-409962; Vinblastine, VBL, NSC-49842; Cyclophosphamide, CTX, NSC-26271; Procarbazine, PCB, NSC-77213; plus Prednisone, PRED, NSC-10023.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy. BVCPP: BCNU; VBL; CTX; PCB; PRED.

STRATIFICATION BY: Participating institutions, age, histology, systemic symptoms.

SPECIAL STUDY PARAMETERS: Tests of liver and kidney function, total protein and electrophoresis, skin tests, staging laparotomy, lymphangiogram.

END POINTS: Response/remission rate, toxicity/morbidity of treatment disease-free interval, survival time.

CURRENT STATUS: 252 patients are to be entered.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 3000 to 4025 rads to each lymph node area over 3.5 to 5 weeks. If residual tumor remains, deliver up to 4000 rads more to a reduced portal. Begin Chemotherapy 1 month following completion of Radiotherapy. BCNU - 100 mg/sqm iv on days 1, 2, 3, 8 and 10; VBL - 5 mg/sqm iv on day 1; CTX - 600 mg/sqm iv on day 1; PCB - 50 mg po on day 1, 100 mg po on day 2, 100 mg/sqm po on days 3 through 10; PRED - 60 mg/sqm/day po on days 1 through 10. Repeat q 28 days for at least 6 cycles, or 3 cycles beyond achievement of complete response.

Arm II: BCNU, VBL, CTX, PCB and PRED as in Arm I. Begin therapy as soon as patient has recovered from laparotomy. Cross over patients with poor response after 3 cycles to Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; PRED - 5 mg and 50 mg tablets; CTX - 100, 200, and 500 mg vials; VBL - 10 mg ampules; PCB - 50 mg capsules.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00030878

8.0009 RADIOTHERAPY AND CHEMOTHERAPY WITH MOPP-BLEO (NM/VCR/BLEO/PCB/PRED) VS A-COPP (ADR/CTX/VCR/PRED/PCB) FOR STAGE III HODGKIN'S DISEASE IN CHILDREN

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PROTOCOL NUMBER(S) SWOG-7612; MDAR-182

OBJECTIVES:

I. Compare the effectiveness of involved field (IF) radiotherapy plus MOPP-BLEO (nitrogen mustard/vincristine/procarbazine/prednisone/low-dose bleomycin) with IF radiotherapy plus A-COPP (adriamycin/cyclophosphamide/VCR/PRED/PCB) chemotherapy for Stage III Hodgkin's disease in children.

II. Determine the patient tolerance of the two chemotherapy regimens in terms of immediate toxicity and the incidence of infection.

III. Determine the late effects of the two treatment regimens with respect to incidence of a) hypothyroidism and sterility, b) cardiopulmonary abnormalities, and c) second malignancies.

PROTOCOL ENTRY CRITERIA: Children under 18 years of age with Stage III Hodgkin's disease, as determined by histology, bilateral lower-extremity lymphangiogram, celiotomy and splenectomy; there must have been no prior treatment.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy and Hormone Therapy plus IF Radiotherapy. MOPP-BLEO: Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023; plus supervoltage irradiation or Cobalt-60.

Arm II: 4-Drug Combination Chemotherapy and Hormone Therapy plus IF Radiotherapy. A-COPP: Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023; plus supervoltage irradiation or Cobalt-60.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Sickle cell preparation, alkaline phosphatase isoenzyme, pulmonary function tests, lymphangiogram, liver/spleen/mediastinum scan, lymphocyte transformation, skin tests, test of immunocompetence, FSH, cardiac sonography, serum copper level, SMA 12/60.

END POINTS: Response/remission rate, progression/recurrence, disease-free interval, recurrence rate, rate of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 138 patients will be entered.

DOSAGE SCHEDULE:

Arm I: MOPP-BLEO: NM - 6 mg/sqm iv, VCR - 1.5 mg/sqm (maximum 2.0 mg) iv; BLEO - 2.0 mg/sqm iv on pre-radiation days 0, 7, 28, 35 and post-radiation days 0, 7, 28, 35, 56, 53, 84, 91; PCB - 100 mg/sqm po daily; PRED - 40 mg/sqm po daily in 4 divided doses, on pre-radiation days 1 through 6, 8-11, 29-34, 36-39 and post-radiation days 1 through 6, 8-11, 29-34, 36-39, 57-62, 64-67, 85-90, 90-95. Follow with the 2nd course on day 29 after the first course. Start Radiotherapy on day 28 following the completion of the 2nd pre-Radiotherapy MOPP-BLEO course with supervoltage irradiation of at least 2 MeV or Cobalt-60 covering an area of 40 x 40 cm at the 80% margin. Irradiate involved regions in the upper torso: 850-1000 rad tumor dose q week for 4 weeks to a total dose of 3500-4000 rads. Rest 4 to 8 weeks. Start irradiation of lower torso at a rate of 750 rad tumor dose q week for 4 weeks. Avoid total dose of over 4000 rads to the spinal cord and the major portion of the heart. Avoid total dose of over 4500 rads to the cauda equina, GI tract, and the upper mediastinum. Maximum total dose to the kidney is 2000 rads. Start first post-Radiotherapy course of MOPP-BLEO on day 56 after Radiotherapy. Follow with the 2nd, 3rd, and 4th courses on post-Radiotherapy days 28, 56, and 84, respectively.

Arm II: A-COPP: ADR - 60 mg/sqm iv on pre-radiation days 0 and 42; 45 mg/sqm iv on post-radiation days 0, 56, 112, and 168. CTX - 300 mg/sqm iv on pre-radiation days 14, 21, 56, 63; 200 mg/sqm iv or po on post-radiation days 14, 21, 70, 77, 126, 133, 182 and 189. VCR - 1.5 mg/sqm (maximum 2.0 mg) iv on pre-radiation days 14, 21, 56, 63 and post-radiation days 14, 21, 70, 126, 133, 182, and 189. PCB - 100 mg/sqm po daily on pre-radiation days 14-28, 56-70; 65 mg/sqm po daily on post-radiation days 14-24, 70-80, 126-136, 182-192. PRED - 40 mg/sqm po daily in 4 doses on pre-radiation days 0-28. Follow with the 2nd course on day 42 of the 1st course. Give Radiotherapy as in Arm I. Start first post-Radiotherapy course of A-COPP on day 56 after Radiotherapy. Follow with the 2nd, 3rd and 4th courses on post-Radiotherapy days 56, 112, and 168, respectively.

Local recurrence within the Radiotherapy treatment field or extension of disease will result in termination of study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 mg and 5 mg vials; NM - 10 mg vials; PCB -50 mg capsules; PRED - 5 mg tablets; BLEO - 15 unit vials; ADR - 10 mg vials; CTX - 200 and 500 mg vials.

DATE SUMMARIZED: 08/76

PATIENT ACCRUAL: 00480279

8.0010 CHEMOTHERAPY WITH MOP-BAP PLUS IMMUNOTHERAPY WITH LEV AND INVOLVED FIELD RADIOTHERAPY FOR STAGES III AND IV HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) SWOG-7808; MDAR-293

OBJECTIVES:

I. Increase the complete remission rate induced with MOP-BAP: nitrogen mustard/vincristine/procarbazine/adriamycin/bleomycin/prednisone alone utilizing involved field radiotherapy in patients with Stages III and IV Hodgkin's disease achieving a partial response (PR) at the end of 6 cycles of MOP-BAP.

II. Determine whether immunotherapy Maintenance with levamisole (LEV) or Consolidation with low-dose, involved field radiotherapy will produce significantly longer remission durations over a no-further-treatment group when complete response (CR) has been induced with 6 cycles of MOP-BAP in Stages III and IV Hodgkin's disease.

PROTOCOL ENTRY CRITERIA: Patients at least 15 years of age with histologically diagnosed Hodgkin's disease classified by the Lukes and Butler system. Patients must have clinical Stages III or IV or pathologic Stage IV according to Ann Arbor criteria. Patients must have adequate cardiac and pulmonary function, and must not have had prior chemotherapy.

PROTOCOL OUTLINE: Randomized study. All patients enter Induction. Patients in complete remission following Induction are randomized to Arm I, Arm II, or Arm III (those with prior radiotherapy are randomized to Arm I or Arm II). Partial responders enter Arm III; those with prior radiotherapy repeat Induction.

Induction: 5-Drug Combination Chemotherapy plus Hormone Therapy. MOP-BAP: Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Adriamycin, ADR, NSC-123127; Bleomycin, BLEO, NSC-125066; plus Prednisone, PRED, NSC-10023.

Arm I: No treatment.

Arm II: Single-agent Immunotherapy. Levamisole, LEV, NSC-177023.

Arm III: Radiotherapy. Involved fields only by supervoltage irradiation of at least 2 MeV or Cobalt-60. Irradiate lymph nodes, liver, lung, and spleen.

STRATIFICATION BY: Bone marrow status, prior radiotherapy, participating institutions. For patients achieving CR following initial therapy: paparotomy or none, initial symptoms, initial bone marrow involvement.

SPECIAL STUDY PARAMETERS: Skin tests for recall antigens, in-vitro lymphocyte reactions, immunoglobulin levels, lymphangiogram, liver biopsy, liver and spleen scan.

END POINTS: Response/remission rate, duration of response, duration of survival, relapse rate.

CURRENT STATUS: 210 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Induction: MOP-BAP: NM - 6 mg/sqm iv on day 1 (3 mg/sqm if bone marrow reserve impaired); VCR - 1.4 mg/sqm iv on days 1 and 8 (2 mg maximum dose); PCB - 100 mg/sqm po on days 2 through 8 and 9 through 12 (50 mg/sqm on days 2 through 8 and 9 through 12 if bone marrow reserve impaired); ADR - 30 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on day 8 (15 mg/sqm if bone marrow reserve impaired); BLEO - 2 mg/sqm (maximum cumulative dose 200 mg/sqm) iv on days 1 and 8; plus PRED - 40 mg/sqm po on days 2 through 8 and 9 through 12 (first and fourth courses only). (Give initial PCB and PRED doses on days 2 through 7, Addendum, December 1978). Repeat q 28 days provided hematologic recovery has taken place for 6 courses. Evaluate after 3 courses. Give nonresponders with minimal myelosuppression increased doses. After 6 courses, remove nonresponders from study, enter PR without prior Radiotherapy to Arm III, randomize CR to Arms I, II, or III. Patients in PR with prior Radiotherapy receive 4 more courses of MOP-BAP. Partial responders continue therapy until complete remission is achieved or relapse.

Arm I: No treatment.

Arm II: LEV - 100 mg/sqm (to nearest 50 mg) each Saturday and Sunday for 2 years.

Arm III: Involved field Radiotherapy to start 6 weeks after day 1 of the last course of Chemotherapy. Lymph nodes - 2000 rads in 2.5 weeks, liver - 1500 rads in 2 weeks, lung - 1000 rads in 2 weeks, spleen - 2000 rads in 3 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: NM - 10 mg vials; VCR - 1 and 5 mg ampules; PCB - 50 mg capsules; PRED - 5, 20 and 50 mg tablets; ADR - 10 mg ampules; BLEO -15 mg vials; LEV - 50 mg tablets.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00170179

8.0011 CHOP CHEMOTHERAPY FOR PATIENTS WITH HODGKIN'S DISEASE - MOPP FAILURES, STAGES III OR IV (7903) OR PREVIOUSLY UNTREATED (7961)

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PROTOCOL NUMBER(S) SWOG-7903/7961

OBJECTIVES:

I. Evaluate the effectiveness, as determined by response rate, of the CHOP (cyclophosphamide/adriamycin/vincristine/prednisone) combination of chemotherapy for remission induction in patients with advanced (Stages III or IV) Hodgkin's disease who have had prior chemotherapy and in those with prior MOPP (no anthracyclines).

II. Assess the length of unmaintained remissions after intensive Induction with ten courses of treatment with CHOP and after documentation of CR by restaging.

III. Evaluate the degree of noncross-resistance of CHOP in MOPP failures in terms of remission induction, duration of remission and survival.

IV. Compare the toxicities and side effects of the CHOP regimen to those of MOPP.

PROTOCOL ENTRY CRITERIA: Patients with histologically diagnosed Hodgkin's disease classified by the Lukes and Butler system, who have adequate pulmonary and cardiac function. Register to Protocol SWOG-7961 patients from the Universities of Arizona or Texas (San Antonio) only, who have Stage III or IV disease (Ann Arbor Classification). These patients must be previously untreated or must be relapsing from prior radiotherapy. Register to Protocol SWOG-7903 patients from any SWOG institution with any stage disease, who have relapsed or failed to respond to one of various MOPP regimens or prior radiotherapy; they may not have had any prior anthracyclines.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Prior therapy: none vs. prior MOPP vs. prior radiotherapy alone; bone marrow reserve: good vs. poor; participating institutions.

SPECIAL STUDY PARAMETERS: KUB lymphangiogram; bone marrow biopsy; if clinically indicated: liver biopsy, sonogram, tumor scans, staging laparotomy, echocardiogram or STI.

END POINTS: Response/remission rate, objective tumor response, duration of response, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: 45 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Enter patients with impaired bone marrow reserve (IBM) (wbc under 4,000, and/or platelets under 100,000, moderate bone marrow infiltration, prior hematologic intolerance to radiotherapy or chemotherapy, or age 65 and above) to reduced dosages as indicated.

CHOP: CTX - 750 mg/sqm (400 mg/sqm for IBM) iv on day 1; ADR - 50 mg/sqm (25 mg/sqm for IBM) iv on day 1; VCR - 1.4 mg/sqm (maximum dose 2 mg) iv on day 1; PRED - 100 mg po on days 1 through 5.

Repeat therapy q 21 days for 10 courses if wbc remains above 3,000 and platelets above 100,000. Remove from study patients with cardiac toxicity due to ADR, patients with increasing disease or Grade 2 or more myelosuppression after 2 courses, patients failing to attain partial responses after 4 courses, and patients with intolerable toxicity reactions to the lowest doses of CTX or ADR. Restage all responders after 10 courses to document residual disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; PRED - 5, 20 and 50 mg tablets; CTX - 100, 200 and 500 mg ampules; VCR - 1 and 5 mg ampules.

DATE SUMMARIZED: 08/79

8.0012 ALTERNATING MOPP (NM/VCR/PCB/PRED) AND SCAB (SZC/CCNU/ADR/BLEO) VS MOPP ALONE FOR ADVANCED HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) BCRP-7808; NCI-78-C-118; NCI-MB-114

OBJECTIVES:

I. Determine whether alternating chemotherapy with MOPP (nitrogen mustard/vincristine/procarbazine/prednisone) and SCAB (streptozotocin/CCNU/adriamycin/bleomycin) offers any significant advantages over therapy with MOPP alone in patients with advanced Hodgkin's disease.

II. Determine whether toxicities of the alternating combinations are greater than with MOPP alone.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven Stage III2A, IIIB, and IV Hodgkin's disease who have not received prior chemotherapy. Patients may not have received prior radiotherapy to the thorax and must have vital capacity or diffusion capacity of at least 75 percent if the deficit results from something other than underlying Hodgkin's disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Hormone therapy alternating with 4-Drug Combination Chemotherapy. MOPP: Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023; alternating with SCAB: Streptozotocin, SZC, NSC-85998; CCNU, NSC-79037; Adriamycin, ADR, NSC-123127; Bleomycin, BLEO, NSC-125066.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. MOPP.

STRATIFICATION BY: Clinical and pathologic stages (CS IA vs. IIA/PS III2A vs. PS IVA; CS IB vs. CS IIB/PS IIIB vs. IVB; CS IIIA/PS III2A vs. PS IVA; CS IIIB vs. IVA vs. IVB/PS IIIB, IVA, or IVB), constitutional symptoms (present vs. absent), participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic parameters, kidney function tests, chest x-ray, KUB, thyroid function tests.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: A total of 157 patients will be randomized.

DOSAGE SCHEDULE:

Arm I: MOPP: NM - 6 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm (maximum 2 mg) iv on days 1 and 8; PCB - 100 mg/sqm/day on days 1 through 14; PRED - 40 mg/sqm/day on days 1 through 14; alternating with SCAB: SZC - 500 mg/sqm/day po on days 29 through 33; CCNU - 100 mg/sqm po on day 29; ADR - 45 mg/sqm iv on day 29 (total cumulative dose not to exceed 550 mg/sqm); BLEO - 15 mg/sqm/day im on days 29 and 36. Cycle to repeat after 7 weeks. PRED to be given with each course of MOPP.

Arm II: MOPP - as in Arm I, courses repeated q 28 days with PRED included in each course.

Continue treatment for a minimum of 3 courses of MOPP/SCAB or 2 courses of MOPP alone. One course of MOPP/SCAB or 2 courses of MOPP alone should be given after attainment of CR. Patients who progress after 1 course of MOPP/SCAB or 2 courses of MOPP alone, those who have a partial response with no further decrease in size of palpable disease, and those who show no change after 3 months of initial treatment should go off study. Patients treated with MOPP alone who do not attain CR will receive SCAB.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

8.0013 RADIOTHERAPY AND CHEMOTHERAPY WITH MOPP (NM/VCR/PCB/PRED) ALONE OR COMBINED FOR EARLY HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) BCRP-7824

OBJECTIVES:

I. Compare remission induction rates in patients with Stages IA, IB, IIA, IIB, and III-1-A Hodgkin's disease treated by megavoltage radiation vs. MOPP chemotherapy (nitrogen mustard/vincristine/-procarbazine/prednisone) vs. MOPP plus radiotherapy.

II. Compare these therapeutic approaches for their long-term control of Hodgkin's disease.

III. Compare the long-term toxicities of these therapeutic modalities with regard to thyroid function, pulmonary function, gonadal function, cardiac function, and bone marrow function.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven Stage IB, IIA, IIB, or III-1-A Hodgkin's disease who are between the ages of 14 and 70 years and who have received no prior treatment. Patients may have extranodal extension of nodal Hodgkin's disease and may have Stage IA mediastinal disease. Patients may not have peripheral nodal Stage IA disease and may not have had prior neoplastic disorders.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. 4 MeV linear accelerator.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. MOPP: Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, 10023. Allopurinol, NSC-1390, is given for bulky disease.

Arm III: Radiotherapy plus 3-Drug Combination Chemotherapy plus Hormone Therapy. 4 MeV linear accelerator plus MOPP.

STRATIFICATION BY: Disease stage: IA (mediastinum), or IIA vs. IB or IIB, vs. III-I-A; size of mediastinal mass: greater or less than one-third of the chest diameter; histology: LP or NS vs. MC or LD.

SPECIAL STUDY PARAMETERS: Hemogram, SMA-12, chest x-ray, thyroid function test, serum LH and FSH.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: About 158 patients will be entered on each arm.

DOSAGE SCHEDULE:

Arm I: 4500 rads over 5 weeks in fractions of 180 rads, 5 fractions per week.

Arm II: MOPP: NM - 6 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm (maximum dose 2.0 mg) iv on days 1 and 8; PCB - 100 mg/sqm po on days 1 through 14; PRED - 40 mg/sqm po on days 1 through 14. Repeat course q 28 days. Continue for at least 6 monthly courses and 2 courses after reaching CR. Continue treatment in PR until 2 courses beyond the maximal response. For bulky disease, give allopurinol - 300 mg/day in 3 divided doses.

Arm III: Radiotherapy as in Arm I followed by 6 monthly courses of MOPP beginning 6 weeks after the last radiotherapy treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

8.0014 CHEMOTHERAPY AND HORMONE THERAPY WITH ADR/DTIC/BLEO/CCNU/PRED (ABDIC) FOR HODGKIN'S DISEASE REFRACTORY TO CONVENTIONAL THERAPY

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PROTOCOL NUMBER(S) MDAR-176

OBJECTIVES:

I. Determine the efficacy of a 5-drug combination chemotherapy program in patients with Hodgkin's disease refractory to conventional MOPP chemotherapy.

II. Define quantitative and qualitative toxicity of this program.

PROTOCOL ENTRY CRITERIA: Previously treated patients with histologically proven diagnosis of Hodgkin's disease, Stages III or IV, and refractory to conventional chemotherapy programs. Patients must have a minimum absolute granulocyte count of 2,000 and a platelet count of a least 100,000.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy plus Hormone Therapy. Adriamycin, ADR, NSC-123127; DTIC, NSC-45388; Bleomycin, BLEO, NSC-125066; CCNU, NSC-79037; Prednisone, PRED, NSC-10023.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

ADR - 45 mg/sqm iv on day 1; DTIC - 200 mg/sqm iv on days 1 through 5; BLEO - 5 mg/sqm iv on days 1 and 5; CCNU - 50 mg/sqm po on day 1; PRED - 60 mg/sqm po on days 1 through 5. Repeat course every 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 12/76

8.0015 COMBINATION CHEMOTHERAPY AND HORMONE THERAPY WITH NM/CTX/PCB/PRED PLUS RADIOTHERAPY FOR GENERALIZED HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) MDAR-37

OBJECTIVES:

I. Increase the remission rate, duration of remission and survival in Stage IIIA and IIIB Hodgkin's disease.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with measurable disease of Stage IIIA or IIIB Hodgkin's disease, who have positive lymphangiograms.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. MOPP: Nitrogen Mustard, NM, NSC-762; Cyclophosphamide, CTX, NSC-26271; Procarbazine, PCB, NSC-77213; plus Prednisone, PRED, NSC-10023; followed by Radiotherapy - Cobalt-60 to mantle, upper two-thirds of the abdomen and pelvis.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Lymphangiogram, pathology review.

END POINTS: Response/remission rate, duration of remission, duration of survival, survival rate, objective tumor response, toxicity/morbidity of therapy.

CURRENT STATUS: About 20 patients will be entered per year.

DOSAGE SCHEDULE:

NM, CTX, PCB and PRED; 2 courses, schedule not given. Allow 3 weeks for hematological recovery, then give Radiotherapy to mediastinum, abdomen, pelvis and peripheral nodes in series, total dose not given. Schedule sequences of doses according to the clinical situation. For upper-torso disease, give 1000 rads/week tumor dose for a minimum tumor dose of 3000 rads, plus additional Radiotherapy within 4 weeks. Shield kidneys after 2000 rads, liver after 2500 rads.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 04/76

8.0016 RADIOTHERAPY ALONE OR WITH COMBINATION CHEMOTHERAPY WITH MOPP (NM/VCR/PCB/PRED) FOR HODGKIN'S DISEASE STAGES I AND II

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PROTOCOL NUMBER(S) UICC-76118; FRE-IGR-H-5; EORTC-H5

OBJECTIVES:

I. Compare in certain groups of Hodgkin's disease heavy initial treatment with high chance of cure, but certain risks, vs. less heavy initial treatment, and second treatment with curative intent in case of relapse.

PROTOCOL ENTRY CRITERIA: Previously untreated patients between 15 and 70 years of age with cytologically verified localized or regional Hodgkin's disease above the diaphragm, clinical Stages I and II (Ann Arbor classification), with or without systemic symptoms.

PROTOCOL OUTLINE: Randomized study. Separately randomize 3 groups of patients. Group A patients (those with histology LP or NS, clinical Stage I and II, age below 40 years and ESR less than 70 mm, laparotomy and spleen negative) are randomized to Arm I and Arm II. Group B patients (as Group A, with positive spleen) and Group C patients (those with histology MC or LD, or Stage II without mediastinal involvement, or age above 40 years, or ESR greater than 70 mm with no laparotomy) are randomized to Arm III or Arm IV.

Arm I: Radiotherapy. Mantle field irradiation only.

Arm II: Radiotherapy. Mantle field irradiation and para-aortic bar.

Arm III: Radiotherapy. Total nodal irradiation.

Arm IV: 3-Drug Combination Chemotherapy and Hormone Therapy. MOPP - Nitrogen mustard NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023; plus Radiotherapy - mantle field irradiation.

STRATIFICATION BY: Participating institutions, histology, age, clinical stages, ESR.

SPECIAL STUDY PARAMETERS: Chest radiograph, bilateral lymphangiography, liver/spleen scan, liver/bone marrow biopsy, laparoscopy, skeletal survey, inferior vena cavagram, liver and kidney function tests, erythrocyte sedimentation rate (ESR).

END POINTS: Response/remission rate, duration of remission, toxicity/morbidity of treatment, survival rate, survival time, nature of relapse, length of disease-free survival, development of secondary malignant disease.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Mantle field irradiation - 4000 rads given in 4 weeks (both sides of neck, both axillae and mediastinum including Th10).

Arm II: Mantle field irradiation - same as in Arm I. After rest period of 2 to 3 weeks, para-aortic irradiation - 4000 rads given in 4 weeks (splenic hilus not included).

Arm III: Mantle field irradiation - same as in Arm I. Rest 4 weeks, then give para-aortic, iliac and inguinal irradiation with spleen or splenic hilus - 4000 rads given in 4 weeks.

Arm IV: Chemotherapy (Routes of drug administration are not given). NM - 6 mg/sqm on days 1 and 8 (maximum 15 mg); VCR - 1.5 mg/sqm on days 1 and 8 (maximum 2 mg); PCB - 100 mg/sqm on days 1 through 10 (maximum 200 mg); PRED - 25 mg/sqm on days 1 through 14 (maximum 60 mg). Repeat course on day 29 and on day 58. Resume Chemotherapy at the end of Radiotherapy in week 19, and repeat week 23 and week 27. Radiotherapy: Start in week 13 from the day of beginning of Chemotherapy, and end in week 16. Mantle field irradiation including Th10 - 3500 rads given in 4 weeks.

Evaluate patients at 2, 4, 6, 9 and 12 months, and then q 6 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

8.0017 CHEMOTHERAPY WITH MOPP (NM/VCR/PCB/PRED) WITH LIMITED OR EXTENDED RADIOTHERAPY FOR HODGKIN'S DISEASE

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PROTOCOL NUMBER(S) UICC-77016

OBJECTIVES:

I. Determine whether good results can be obtained and maintained with less intensive therapy for Hodgkin's disease.

II. Determine whether the proposed chemotherapy with MOPP prior to and both before and after radiotherapy is curative for subclinical lesions.

III. Compare a limited vs. extensive radiotherapy combined with MOPP chemotherapy.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with biopsy-proven Stage I and II Hodgkin's disease including patients with Stage III A adenopathies above and below the diaphragm but without liver involvement.

PROTOCOL OUTLINE: Randomized study.

Enter all patients to Regimen A, then separately randomize patients in 3 groups: Group A: patients less than 40 years of age, with histological types 1 or 2, clinical topographic Stage I or II with mediastinal involvement, and without symptoms of general malaise; Group B: patients more than 40 years of age, with histological types 3 or 4 and clinical topographic Stage II without mediastinal involvement and with symptoms of general malaise; Group C: Group B patients with Stage III A nodal status with adenopathies above and below the diaphragm. Following treatment on Arm I or II, Group B and Group C patients enter Regimen B.

Regimen A: 3-Drug Combination Chemotherapy and Hormone Therapy. MOPP: Nitrogen mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023, or Prednisolone, PRDL, NSC-9900.

Arm I: Extended Radiotherapy.

Arm II: Limited Radiotherapy.

Regimen B: Postirradiation 3-Drug Combination Chemotherapy and Hormone Therapy. MOPP.

STRATIFICATION BY: Age, histological grade, disease stage, clinical symptoms, extent of disease, participating institutions.

SPECIAL STUDY PARAMETERS: Bone marrow exam, ganglion biopsy, toxoplasmosis, chromosome analysis.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, recurrence rate, iatrogenic morbidity.

CURRENT STATUS: A minimum of 134 patients in Group A and a minimum of 90 patients in Group B will be entered.

DOSAGE SCHEDULE:

Regimen A: NM - 6 mg/sqm on days 1 and 8; VCR - 1.4 mg/sqm on days 1 and 8; PCB - 1100 mg/sqm on days 1 through 14; PRED or PRDL - 40 mg/sqm on days 1 through 14 for the first course, then tapered over 4 days and repeated in the 3rd course for Group B. Repeat course q 14 days for 3 courses. Fifteen days following the completion of Chemotherapy, enter randomized patients to Radiotherapy, Arm I or Arm II.

Arm I: 4000 rads total dose given in 25 to 30 days to total nodal areas, the supradiaphragmatic mantle and para-aortic region (to L4-L5), with additional coverage of subdiaphragmatic regions as required by the extent of the disease. For Group C patients, irradiate all nodal areas above and below the diaphragm (mantle and inverse Y).

Arm II: 4000 rads total dose given in 25 to 30 days to clinically involved nodal areas only. An additional 5000 to 1000 rads may be given to residual tumor-bearing nodes in Arms II or III.

Regimen B: 30 days following Radiotherapy, enter Group B and Group C patients only to 3 additional courses of MOPP, as in Regimen A, with a possible additional 1 or 2 courses.

Follow up all patients q 3 months to the end of the second year, q 6 months to the end of the fifth year and then once a year indefinitely. Patients who relapse are treated by additional radiotherapy followed after 1 or 2 months by 6 monthly courses of the ABVD (Bonadonna, 1976) regimen.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

8B. NON-HODGKIN'S LYMPHOMA AND OTHER SPECIFIED LYMPHOMAS

8.0018 PHASE III STUDY OF RADIOTHERAPY PLUS CHEMOTHERAPY WITH COMP VS MODIFIED LSA2-L2 FOR NON-HODGKIN'S LYMPHOMA IN CHILDREN

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PROTOCOL NUMBER(S) CCG-551

OBJECTIVES:

I. Study the classification and biology of that group of childhood neoplasms included in the 'Non-Hodgkin's Lymphomas'.

II. Compare the effectiveness of two combination chemotherapy programs in the control of all forms of childhood non-Hodgkin's lymphoma:

A. Pulsed High Dose Cyclophosphamide, Moderate Dose Methotrexate, Vincristine and Prednisone (COMP), vs.

B. The Memorial Hospital LSA2-L2 Protocol (Modified).

III. Determine for each of the two treatment regimens the effectiveness of standardized IT MTX without radiation for the control of occult CNS disease.

IV. Determine for each of the treatment regimens the effectiveness of standardized irradiation of bulk disease.

PROTOCOL ENTRY CRITERIA: Previously untreated patients under 18 years of age with non-Hodgkin's lymphoma histologically diagnosed according to Rappoport's classification. Patients must have no blast cells in the peripheral blood and not more than 25 percent in the bone marrow. 'Good prognosis' patients are identified by disease confined to primary sites with limited extension to lymph nodes and other specified sites; 'poor prognosis' patients will be all others not so specified.

PROTOCOL OUTLINE: Randomized study.

Following biospy or resection randomize patients to Arm I or Arm II. (Arm I closed to 'good prognosis' patients, Addendum 12, March 1979.) (Patients with mediastinal mass at diagnosis will not be randomized but will be treated with Arm II. Addendum 15, March 1980.) (Addendum 15 cancelled by Addendum 17, July 1980.)

Addendum 14, March 1980: All 'good' prognosis patients will receive treatment with COMP for either 6 months (induction plus not less than five 28-day cycles of COMP maintenance) or 18 months (induction plus not less than seventeen 28-day cycles of COMP maintenance). The duration of treatment will be randomly chosen after completion of 6 months treatment. This randomization will be effective April 1, 1980, for 'good' prognosis patients who began treatment after October 1, 1979. (Effective August 1980, treatment randomization for patients with non-localized disease will be discontinued. Patients with lymphoblastic lymphoma will be assigned to treatment with LSA2-L2 and those with nonlymphoblastic lymphoma to COMP. Addendum 17, July 1980.)

Arm I:

Induction: Radiotherapy - Cobalt 60 or radiation beams of equivalent or higher energies - to all tumor sites with tumor mass greater than 3.0 cm in diameter at diagnosis, and, for CNS disease, to the whole brain, associated meninges and to the spinal cord to the level of the second cervical vertebra.

Induction and Maintenance: 3-Drug Combination Chemotherapy plus Hormone Therapy. COMP: Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; plus Prednisone, PRED, NSC-10023.

Arm II:

Induction: Radiotherapy - as in Arm I, plus 4-Drug Combination Chemotherapy and Hormone Therapy. LSA2-L2: CTX, VCR, MTX, Daunomycin, DNM, NSC-82151; plus PRED. Consolidation: 5-Drug Combination Chemotherapy. Cytosine Arabinoside, ARA-C, NSC-63878; 6-Thioguanine, TG, NSC-752; L-Asparaginase, L-ASP, NSC-109229 or NSC-106977; BCNU, NSC-409962; and MTX. Maintenance: Sequential 8-Drug Combination Chemotherapy. Each course consists of 5 treatment cycles lasting 5 days each, separated by 7 days rest, in the following order: TG plus CTX; Hydroxyurea, HU, NSC-32065, plus DNM; MTX plus BCNU; ARA-C plus VCR; MTX-IT.

STRATIFICATION BY: Extent of disease: localized vs. regional; anatomical site; histology (modified Rappoport classification); bone marrow status; CNS disease; age: over vs. under 13 years of age; participating institutions.

SPECIAL STUDY PARAMETERS: CSF examination, including cytology; IVP; lymphangiogram; skeletal survey; liver, spleen, bone and gallium scans; T and B cell markers; EBV titer.

END POINTS: Response/remission rate, survival time, survival rate, toxicity/morbidity of treatment, CNS relapse rate, response and relapse rates on days 35 and 100, relapse in irradiated tissue, disease site at relapse.

CURRENT STATUS: About 320 patients will be entered in 4 to 4.25 years.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 2000 rads in 10 to 20 fractions for 'poor prognosis' patients, 3000 rads in 15 to 20 fractions for 'good prognosis' patients beginning on days 3 to 7, or, if bone marrow toxicity is anticipated, as soon as possible after day 20, when bone marrow has recovered from MTX therapy. CNS disease: Begin cranial irradiation on day 1 of chemotherapy for CNS disease present at diagnosis, for isolated relapse during systemic remission or CNS relapse during induction - 2400 rads given in 12 fractions in 2 to 2.5 weeks. Subsequent cranial irradiation will have priority over any other treatment in the event of competitive toxicity.

Chemotherapy. Induction: CTX - 1.2 mg/sqm iv on day 1; VCR - 2.0 mg/sqm (maximum 2.0 mg) iv on days 3, 10, 17 and 24; PRED - 60 mg/sqm/day (maximum 60) po in 4 divided doses beginning on day 3 and continued for 28 days, then taper to discontinue on day 37; MTX - 300 mg/sqm iv on day 12, plus 6.25 mg/sqm intrathecal (IT) on days 5, 31 and 34. Delay MTX if granulocyte count is below 500; reduce dosage if count below 1000. Remove from study patients with progressive disease during hematological recovery.

Maintenance: Begin following completion of induction therapies, between 7 and 21 days after the last dose of MTX-IT, provided absolute granulocyte count is above 1500. CTX - 1.0 mg/sqm iv on day 1 and q 28 days thereafter; VCR - 1.5 mg/sqm iv on day 1 and q 14 days thereafter; PRED - 60 mg/sqm/day po for 5 days beginning on day 29 and q 28 days thereafter; MTX - 300 mg/sqm (60% of the calculated dose given iv push and 40% as iv infusion–Addendum 16, March 1980) on day 15 and q 28 days thereafter, plus 6.25 mg/sqm it on day 29 and q 28 days thereafter. Repeat course q 28 days for 18 months or until systemic relapse.

Arm II: (Enter only 'poor prognosis' patients, Addendum 12.)

Radiotherapy, as in Arm I.

Chemotherapy. Induction: CTX, VCR, MTX-IT only, PRED, as in Arm I, plus DNM - 60 mg/sqm iv on days 12 and 13. Delay DNM if the absolute granulocyte count is less than 1,000. Remove from study patients with progressive disease during hematological recovery.

Consolidation: Begin following completion of induction therapies, between 7 and 21 days after the last dose of MTX-IT, provided the absolute granulocyte count is above 1000. ARA-C - 100 mg/sqm iv on days 1 through 5 q 7 days for 4 weeks, or 3 weeks if absolute granulocyte count falls below 1000. TG -50 mg/sqm po 8 to 12 hours after each dose of ARA-C. If absolute granulocyte count is above 1500, give TG 7 days a week. If ARA-C is discontinued, discontinue TG at the same time. L-ASP - 6000 IU/sqm/day im (or, in case of allergy, use L-ASP, NSC-106977 -2000 IU/sqm/day, Addendum June 1977 amended to 6000IU/sqm/dose, November 1978) for 14 days. Monitor lipase and amylase levels, pancreatic size by sonography, and discontinue if hyperglycemia develops. MTX - 6.25 mg/sqm it on days 1 and 3 beginning 2 to 3 days after the last L-ASP injection; BCNU - 60 mg/sqm iv single dose 2 to 3 days following completion of MTX-IT therapy.

Maintenance: Begin 7 to 14 days following completion of Consolidation, provided the absolute granulocyte count is at least 1000. Delay each successive cycle until granulocyte count reaches this level (Amendment 1, June 1977). Cycle 1. TG - 300 mg/sqm/day po on days 1 through 4; CTX - 600 mg/sqm iv single dose on day 5. Cycle 2. HU -2400 mg/sqm/day po on days 1 through 4; DNM - 45 mg/sqm iv single dose on day 5. Cycle 3. MTX - 10 mg/sqm/day po on days 1 through 4; BCNU -60 mg/sqm iv single dose on day 5. Cycle 4. ARA-C - 150 mg/sqm/day iv on days 1 through 4; VCR - 2.0 mg/sqm iv single dose on day 5. Cycle 5. MTX - 6.25 mg/sqm IT, on day 1 and day 3. Rest 10 days, then repeat course beginning with Cycle 1, and continue therapy for 18 months or until systemic relapse. Give a minimum of 5 courses maintenance therapy, continuing beyond 18 months if necessitated by earlier delays because of toxicity. Follow all patients for 5 years or until death.

Dosage modifications for toxicity and CNS disease are given.

DOSAGE FORMS: CTX - 200 and 500 mg vials; VCR - 1 and 5 mg vials; PRED - 5 mg tablets; MTX - 50 mg vials; DNM - 20 mg vials; ARA-C - 100 and 500 mg vials; TG - 40 mg tablets; L-ASP - 10,000 and 5,000 IU vials; BCNU - 100 mg vials; HU - 500 mg capsules.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 01100279

8.0019 PHASE III INDUCTION WITH COPA VS COPA/BLEO & CONSOLIDATION WITH HIGH DOSE MTX/CF VS MTX FOR DIFFUSE HISTIOCYTIC AND LYMPHOCYTIC LYMPHOMA

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PROTOCOL NUMBER(S) CLB-7851

OBJECTIVES:

I. Compare the effect of Induction with COPA: cyclophosphamide (CTX), adriamycin (ADR), vincristine (VCR), prednisone (PRED) vs. COPA plus bleomycin (BLEO) for advanced, diffuse, histiocytic lymphoma.

II. Compare the effect of consolidation with high dose methotrexate with citrovorum rescue (MTX-CF) vs. conventional MTX.

PROTOCOL ENTRY CRITERIA: Patients between 16 and 70 years of age with histologically confirmed, measurable Stage II or IV diffuse, histiocytic and lymphocytic lymphoma. Patients must have life expectancy greater than 6 weeks, an ECOG performance status of less than 4, and adequate hematologic, pulmonary, liver, kidney and cardiac function. Patients must not have had prior chemotherapy, extensive radiotherapy and they may not have lymphomatous CNS involvement.

PROTOCOL OUTLINE: Randomized study for Induction and Consolidation.

Induction:

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. COPA: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; plus Prednisone, PRED, NSC-10023.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy. COPA, as in Arm I; plus Bleomycin, BLEO, NSC-125066.

Consolidation: Rerandomize patients in partial or complete remission.

Arm III: 2-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

Arm IV: Single-agent Chemotherapy. MTX.

After Consolidation: Re-enter all patients in partial or complete remission to Arm I.

STRATIFICATION: Participating institutions. For consolidation only–response: complete vs. partial; induction treatment: COPA vs. COPA/BLEO.

SPECIAL STUDY PARAMETERS: Lesion measurement; liver, kidney, and pulmonary function; liver and bone scan; bone marrow aspirate and bilateral biopsies; lymphangiogram; liver scan, if any indication of abnormality; lumbar puncture with cytology; IVP; CAT scan.

END POINTS: Response/remission rate, duration of response, time to onset of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, CNS involvement.

CURRENT STATUS: 250 patients will be entered in more than 3 years.

DOSAGE SCHEDULE:

Induction:

Arm I: COPA: CTX - 750 mg/sqm iv bolus on day 1; ADR - 250 mg/sqm iv bolus on day 1; VCR - 1.4 mg/sqm (maximum 2 mg) iv bolus on day 1; PRED - 100 mg/sqm po on days 1 through 5.

Arm II: COPA as in Arm I; BLEO - 2U/day iv continuous infusion on days 1 through 5. Repeat induction courses q 21 days for 3 courses. Re-evaluate patients after recovery from third course and remove from study patients who do not show partial or complete response.

Consolidation: Re-randomize responders to enter Arm III or IV on day 64.

Arm III: MTX-CF: MTX - 3 gm/sqm iv given over 20 minutes on day 1; followed 24 hours later by CF - 10 mg/sqm iv on day 2, then by 10 mg/sqm po or iv q 6 hours for 12 doses.

Arm IV: MTX - 30 mg/sqm po q 7 days.

Repeat consolidation courses q 7 days for 3 courses. Re-evaluate 1 week after third course.

After consolidation: Enter all patients from consolidation to Arm I no later than 10 days after the third and last course of consolidation therapy. Repeat q 21 days for 3 courses. Give no further therapy to patients in complete remission but re-evaluate q 3 months. Remove patients in partial remission or with disease progression from study.

Dosage modifications for toxicity and for patients with hepatic or urinary dysfunction are given.

DOSAGE FORMS: ADR - 10 or 50 mg vials; VCR - 1 and 5 mg ampules; BLEO - 15 unit ampules; MTX - 50, 500 and 1000 mg vials; CF - 3 and 50 mg vials; CTX - 100, 200 and 500 mg vials.

DATE SUMMARIZED: 10/79

8.0020 PILOT CHEMOTHERAPY WITH MTX/VM-26/PCB/DM FOR REFRACTORY, POOR HISTOLOGY OR NODULAR, POORLY DIFFERENTIATED LYMPHOCYTIC LYMPHOMA

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PROTOCOL NUMBER(S) CLB-7902

OBJECTIVES:

I. Determine the effects of methotrexate (MTX) with citrovorum factor rescue/VM-26/procarbazine (PCB)/dexamethasone (DM) on nodular, poorly differentiated lymphocytic, diffuse poorly differentiated lymphocytic, diffuse mixed histiocytic-lymphocytic, or diffuse histiocytic lymphoma refractory to prior therapy.

II. Evaluate effects of VM-26 and PCB on the pharmodynamics of MTX.

PROTOCOL ENTRY CRITERIA: Patients at least 16 years of age with histologically confirmed, measurable, Stage III or IV nodular poorly differentiated lymphocytic, diffuse poorly differentiated lymphocytic, diffuse mixed histiocytic-lymphocytic or diffuse histiocytic lymphoma who are in relapse from or have failed to respond to conventional chemotherapy. Patients must have a performance status of at least 3, a life expectancy of at least 6 weeks, and adequate hematologic, cardiac, liver, and kidney function. Patients must not have had prior chemotherapy with VM-26 or high dose MTX, myelosuppressive chemotherapy in the previous 2 weeks or radiotherapy or nitrosourea therapy in the preceding 4 weeks, or previous extended field or total body irradiation.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. MVPD-26: Methotrexate, MTX, NSC-740 with Citrovorum factor, CF, NSC-3590; VM-26, NSC-122819; Procarbazine, PCB, NSC-77213; Dexamethasone, DM, NSC-34521.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Liver and bone scans, bone marrow aspirate and bilateral biopsies, liver biopsy, lumbar puncture with SF cytology, upper GI and small bowel series, IVP, lymphangiogram, abdominal sonogram or CT scan.

END POINTS: Response/remission rate, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: About 20 patients will be entered.

DOSAGE SCHEDULE:

MVPD-26: MTX (if kidney function is at least 50% of normal) - 100 mg/sqm one-third iv rapid injection and two-thirds iv continuous infusion over 1 hour on day 1 with adequate hydration 24 hours prior, concurrent, and 48 hours after MTX administration; CF - 10 mg/sqm iv 24 hours after MTX, then iv or po q 6 hours for 12 doses or none if serum MTX is less than 2 x 10 to the minus eighth power molar; VM-26 - 100 mg/sqm iv continuous infusion over 1 hour on days 2 (following CF) and 9; PCB - 100 mg/sqm po in 3 divided doses on days 2 through 15 after VM-26; DM -15 mg/day po in 4 divided doses on days 2 through 8, all given q 28 days after 3 courses. (All patients who do not experience Grade III or IV leukopenia and/or thrombocytopenia receive VM-26 at 120 mg/sqm in the second and subsequent courses. Addendum 1, April 1980.) Remove from study patients who are in progression or relapsed after 3 courses, and give 3 more courses to patients with complete or partial remission or stable disease. After a total of 6 courses, remove from study patients in progression or relapse, and continue therapy for rest of the patients q month until relapse or disease progression.

Dosage modifications for toxicity, impaired kidney function or ascites are given.

DOSAGE FORMS: VM-26 - 50 mg vials; MTX - 5 or 50 mg vials; CF - 3 and 50 mg vials; PCB - 50 mg capsules; DM - 0.75, 2.0, and 4.0 mg tablets.

DATE SUMMARIZED: 09/79

8.0021 PHASE III CHEMOTHERAPY WITH CTX VS CTX/ADR/VCR/BLEO/PRED FOR STAGES III AND IV NODULAR POORLY DIFFERENTIATED LYMPHOCYTIC LYMPHOMA

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PROTOCOL NUMBER(S) CLB-7951

OBJECTIVES:

I. Compare effects of cyclophosphamide (CTX) vs. CTX/adriamycin (ADR)/ vincristine (VCR)/bleomycin (BLEO)/prednisone (PRED) on Ann Arbor Stage III and IV, lymphocytic, poorly differentiated nodular (LPDN) and lymphocytic, poorly differentiated nodular and diffuse (LPDND) lymphoma.

II. Determine what percentage of patients with LPDN are asymptomatic.

III. Determine influence of degree of nodularity on response.

PROTOCOL ENTRY CRITERIA: Patients at least 16 years of age with histologically-confirmed, measurable, Ann Arbor Stage III or IV lymphocytic, poorly differentiated, nodular or nodular and diffuse lymphoma. Patients must: be previously untreated with radiotherapy or chemotherapy (except less than 1 month of corticosteroid therapy); be entered in study within 3 months of diagnosis; have performance status of at least 3, life expectancy of more than 6 weeks, and adequate kidney function; and unless due to the lymphoma, have adequate hematologic, liver, and lung function. Patients must not have lymphomatous involvement requiring immediate radiotherapy.

PROTOCOL OUTLINE: Randomized study for Induction only.

Induction and Maintenance:

Arm I: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy. CTX; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066; plus Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Participating institutions; age: up to 70 vs. over 70; deferred treatment candidate: yes vs. no.

SPECIAL STUDY PARAMETERS: Lesion measurement; CBC and differential platelet counts, electrolytes; liver, kidney, and pulmonary function; uric acid and urinalysis; liver and bone scan; bone marrow aspirate and biopsy; liver biopsy; lumbar puncture; upper G.I. and small bowel series; intravenous pyelogram; abdominal sonogram or CT scan; lymphangiogram; surface markers.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 214 patients will be entered in 2.5 years.

DOSAGE SCHEDULE:

Induction and Maintenance:

Arm I: CTX - 100 mg/sqm/day po. Evaluate patients q 3 weeks during Induction. Enter patients with progressive disease after 6 weeks or no response after 9 weeks to Arm II. Continue remaining patients on therapy and evaluate at 18 weeks. Continue patients with complete response at 18 weeks on therapy for 2 years and evaluate q 4 weeks. Continue patients with partial remission at 18 weeks on therapy as long as there is no tumor progression, evaluate q 3 months, and continue therapy for 2 years after patient achieves complete remission. Discontinue therapy after 2 years of continuous complete remission. Enter patients who relapse or progress while on therapy or who relapse within 6 months after discontinuing therapy to Arm II. Reenter patients who relapse more than 6 months after discontinuing therapy to Arm I.

Arm II: All patients randomized to Arm II enter Arm IIA. (A) CTX - 750 mg/sqm iv bolus on day 1; ADR - 50 mg/sqm iv bolus on day 1; VCR - 1.4 mg/sqm (maximum dose 2 mg) iv bolus on day 1; BLEO - 10 units/sqm (maximum cumulative dose 300 units) im on day 1; PRED - 60 mg/sqm po on days 1 through 5; all q 3 weeks. (B) As in A except eliminate BLEO; all q 4 weeks. (C) As in B except eliminate ADR and increase CTX to 1000 mg/sqm; all q 4 weeks. Evaluate patients before each Arm IIA cycle. Remove from study patients with progressive disease after 2 cycles or no response after 3 cycles. Evaluate remaining patients at 18 weeks. Enter patients in complete remission at 18 weeks to Arm IIB until a cumulative dose of ADR equals 450 mg/sqm, then continue on Arm IIC: For patients in complete remission continue therapy for 2 years, and discontinue therapy for patients who remain in continuous complete remission for 2 years. Enter patients who are in partial remission at 18 weeks to Arm IIB until complete remission is attained or cumulative dose of ADR equals 450 mg/sqm. Then enter patients still in partial remission to Arm IIC and reevaluate q 3 months. Treat patients who achieve complete remission on Arm IIB or after 6 cycles of Arm IIC as above. Reenter patients who relapse less than 6 months after Chemotherapy has been discontinued to Arm II, and remove from study patients who relapse at 6 months or later.

Evaluate patients q 3 months after therapy is discontinued. Remove from study patients in progression at any time during therapy. Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials, 1 and 5 mg ampules; BLEO - 15 U ampules; PRED - 2.5, 5, 10, 20 and 50 mg tablets.

DATE SUMMARIZED: 02/80

8.0022 PHASE III CTX/PRED INDUCTION AND CONSOLIDATION VS RADIOTHERAPY CONSOLIDATION FOR STAGE III OR IV NODULAR NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) EST-4477

OBJECTIVES:

I. Achieve a high incidence of partial and complete responders for Stages III and IV prognostically favorable (nodular) histologic subtypes of non-Hodgkin's lymphoma using nonaggressive, well-tolerated induction chemotherapy with cyclophosphamide (CTX) plus prednisone (PRED). (Patients with nodular histiocytic subtype are no longer eligible. Addendum 5, December 1979.)

II. Compare an additional four cycles of induction chemotherapy with low-dose radiotherapy to all sites of pretreatment involvement (except bone marrow) in terms of: a) increasing the percentage of complete remissions; b) prolonging the duration of remission and survival; and c) decreasing the incidence of uncontrollable abdominal lymphoma.

III. Determine whether there are differences in overall survival and remission duration between complete and partial remissions in non-Hodgkin's lymphomas of favorable histologies.

IV. Determine the ease of administration and toxicity of low-dose radiotherapy following eight cycles of induction chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with histologically diagnosed, measurable, progressive and/or symptomatic, clinical Stages III A, III B, IV A, and IV B (Ann Arbor classification) malignant lymphoma of the following subtypes: nodular lymphocytic, well differentiated or poorly differentiated; nodular mixed; or nodular histiocytic. (Nodular histiocytic subtype no longer eligible. Addendum 5, December 1979.) Patients must have adequate blood cell counts, adequate kidney function, and fewer than five separate bone lesions. Patients must not have had prior chemotherapy, except for prednisone; total body, total nodal, or whole abdominal irradiation; and recurrence of lymphoma in an area which has been exposed to radiotherapy exceeding 2000 rads. All known involved anatomic areas must be accurately mapped before initiation of chemotherapy.

PROTOCOL OUTLINE: Randomized study for Consolidation only.

Induction:

Regimen A: Single-agent Chemotherapy plus Hormone Therapy. Cyclophosphamide, CTX, NSC-26271; plus Prednisone, PRED, NSC-10023.

Consolidation: Randomize patients to Arm I or Arm II.

Arm I: Single-agent Chemotherapy plus Hormone Therapy. CTX/PRED, as in Regimen A.

Arm II: Radiotherapy. Low dose, megavoltage to all sites of pretreatment involvement.

STRATIFICATION BY: Participating institutions; for Consolidation: response to Induction therapy, bone marrow status, stage at initial registration.

SPECIAL STUDY PARAMETERS: Protein electrophoresis, bipedal lymphangiogram, bilateral iliac crest, bone marrow and liver biopsies, computerized axial tomography and ultrasound scan, bone x-rays, IVP.

END POINTS: Objective tumor response, response/remission rate, duration of response, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: About 244 patients will be entered in about 33 months.

DOSAGE SCHEDULE:

Induction:

Regimen A: CTX - 600 mg/sqm iv on days 1 and 8; PRED - 100 mg/sqm po on days 1 through 5 q 28 days for 8 courses.

Remove from study patients with progressive disease following 2 courses of Induction.

Consolidation: Enter randomized patients with partial or complete response.

Arm I: CTX; plus PRED dosage as in Regimen A for 4 courses. Observe patients until progression or relapse.

Arm II: Begin Radiotherapy one month after completion of Induction, if blood counts are adequate. For complete responders: irradiate all sites of pretreatment involvement, except bone marrow, if involved. Treat whole abdomen, including liver and spleen, if pretreatment lymphangiogram was positive: 1500 rads given at escalating daily fractions to 150 rad/day on 5 days/week. To entire involved organs: to lung or kidney give a total dose of 1500 rads with daily fraction of 150 rads; to nodal sites, liver, bone and skin sites, 1500-2000 rads at 150-200 rads/day. Divide dose with 2 to 4 week rest period if both supra-and infra-diaphragmatic sites are involved. For partial responders: treat as above for complete responders except to areas of persistent disease give 3000 rads total dose at 150 to 200 rads/fraction on 5 days/week. Observe all patients until progression or relapse and for survival.

Evaluate patients in restaged complete remission (liver biopsy evidence) q 2 months for 1 year, then q 3 months. Evaluate patients in clinical complete or partial remission q month for 1 year, than q 2 months thereafter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PRED - 5, 20 and 50 mg tablets; CTX - 200 and 500 mg vials.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00800579

8.0023 PHASE III COPA VS COPA & BLEO VS CAP-BOP & RADIOTHERAPY CONSOLIDATION FOR UNFAVORABLE HISTOLOGIC SUBTYPES OF NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) EST-5477

OBJECTIVES:

I. Compare 4-drug combination chemotherapy with COPA: cyclophosphamide (CTX)/adriamycin (ADR)/vincristine (VCR) plus prednisone (PRED) to 5-drug combination chemotherapy with COPA-bleomycin (BLEO) to 6-drug combination chemotherapy with CAP-BOP: CTX/ADR/procarbazine (PCB)/BLEO/VCR/PRED as induction therapy for prognostically unfavorable malignant lymphomas.

II. Determine the effect of radiation as consolidation therapy.

PROTOCOL ENTRY CRITERIA: Patients with Stage IIIa, IIIb, IVa, or IVb (Ann Arbor classification), tissue-diagnosed, measurable, malignant lymphoma of one of the following types only: diffuse lymphocytic, diffuse mixed, diffuse histiocytic, diffuse undifferentiated with diagnosis confirmed by Lymphoma Panel. Patients must have adequate renal function and adequate hematologic function; however, patients with biopsy-proven malignant lymphoma invasion of bone marrow may enter with wbc between 2000 and 4000 or platelet count between 75,000 and 100,000. Patients must not have had prior treatment with cytotoxic Chemotherapy, recurrence of lymphoma after prior radiation therapy, severe, non-neoplastic pulmonary disease, active heart disease, and other serious medical conditions which preclude aggressive cytotoxic Chemotherapy. Do not enter patients with more than 15,000 wbc where more than 50% of cells in peripheral blood are lymphocytes and/or 25% are lymphoblasts and patients with 5 or more bone or skin sites involved which cannot be treated with radiation as outlined in protocol.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. COPA: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; plus Prednisone, PRED, NSC-10023.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy. COPA plus BLEO: CTX; ADR; VCR; PRED plus Bleomycin, BLEO, NSC-125066.

Arm III: 5-Drug Combination Chemotherapy plus Hormone Therapy. CAP-BOP: CTX; ADR; Procarbazine, PCB, NSC-77213; BLEO; VCR; PRED.

Consolidation: Randomize all patients who have had a complete response during first 24 weeks of treatment and who continue to be in complete remission, to Arms IV and V.

Arm IV: Observe patients.

Arm V: Megavolt irradiation to all sites of pretreatment involvement.

STRATIFICATION BY: Participating institutions; histology: diffuse histiocytic vs. other; induction; performance status: 0-1 vs. 2-4; disease stage: III vs. IV; Consolidation; Induction phase treatment: Arm I vs. Arm II vs. Arm III.

SPECIAL STUDY PARAMETERS: Bilateral iliac crest bone marrow biopsy, liver and kidney function tests, chest X-ray, bipedal lymphangiogram, plain film of abdomen, IVP and gastrointestinal X-rays, liver biopsy, radioisotopic scans, lumbar puncture for cytology.

END POINTS: Objective tumor response, duration of response, length of survival, toxicity/morbidity of treatment, response/remission rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction:

Arm I: COPA: CTX - 600 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; VCR - 1.2 mg/sqm (maximum 2.0 mg) iv on day 1; PRED - 100 mg/sqm/day po on days 1 through 5. Repeat course q 21 days for 8 courses.

Arm II: COPA-BLEO: COPA, as in Arm I, except give VCR on day 15; BLEO - 10 mg/sqm im on day 15. Repeat course q 21 days for 8 courses.

Arm III: CAP-BOP: CTX - 500 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 1; PCB - 100 mg/sqm po on days 1 through 7; BLEO - 10 mg/sqm im on day 15; VCR - 1.2 mg/sqm iv on day 15; PRED - 40 mg/sqm/day po on days 15 through 21. Repeat course q 28 days for 6 courses.

Remove from study patients with disease progression after 1 cycle of therapy, no change after 12 weeks of therapy, or partial response after 24 weeks of therapy. Systematically restage all complete responders, then randomize to Consolidation (Addendum 5, August, 1979).

Consolidation:

Arm IV: No treatment.

Arm V: Restage patients eligible for Consolidation. Begin radiation 8 weeks after completion of Induction therapy (Addendum 5, August 1979) or as soon as hematologic function is adequate. Give 1500 to 3000 rads depending on area of involvement. Irradiate all (and only) sites of pretreatment involvement (except bone marrow). Interrupt Radiotherapy if wbc falls below 2000 and/or platelets below 50,000.

Observe patients q 2 months in the first year, q 3 months in the second year, and q 4 months thereafter until relapse, then remove patients from study who relapse, but follow for survival data.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 200 and 500 mg vials; VCR - 1 and 5 mg vials; PRED - 5, 10 and 20 mg scored tablets; BLEO - 15 unit ampules; ADR - 10 and 50 mg vials; PCB - 50 mg capsules.

DATE SUMMARIZED: 10/79

PATIENT ACCRUAL: 00880679

8.0024 PHASE III CHEMOTHERAPY WITH BCOP (BCNU/CTX/VCR/PRED) VS CHOP (CTX/ADR/VCR/PRED) FOR NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) SEG-77NHL0103; SEG-77NHL317

OBJECTIVES:

I. Compare the response rate, response duration and survival of patients treated with BCOP: BCNU/cyclophosphamide (CTX)/vincristine (VCR)/prednisone (PRED) vs. CHOP: CTX/adriamycin (ADR)/VCR for non-Hodgkin's lymphoma.

II. Determine whether patients failing on one regimen will subsequently respond to therapy with the other regimen.

PROTOCOL ENTRY CRITERIA: Patients with measurable disease of biopsy-proven nodular histocytic or diffuse non-Hodgkin's lymphoma (except well-differentiated), Stages II, III, or IV. Patients with diabetes, tuberculosis, peptic ulcer or controlled CNS involvement may be included. Patients must not have had prior chemotherapy but may have had minimal radiation.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. BCOP: BCNU, NSC-409962; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: CTX; Adriamycin, ADR, NSC-123127; VCR; PRED.

STRATIFICATION BY: Prior therapy, histological diagnosis, participating institutions.

SPECIAL STUDY PARAMETERS: Liver function tests, bone and liver-spleen scans, EKG, bone marrow biopsy, lymphangiogram.

END POINTS: Response/remission rate, duration of remission, survival time, objective tumor response, survival rate.

CURRENT STATUS: About 200 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: BCOP: BCNU - 100 mg/sqm iv on day 1; CTX - 600 mg/sqm iv on day 1; VCR - 1 mg/sqm on days 1 and 5; PRED - 100 mg/sqm/day po for 10 days. Repeat course q 28 days for 6 courses.

Arm II: CHOP: CTX - 600 mg/sqm iv on day 1; ADR - 50 mg/sqm (maximum cumulative dose 450 mg/sqm) iv on day 1; VCR - 1 mg/sqm iv days 1 and 5; PRED - 100 mg/sqm/day for 5 days. Repeat course q 21 days for 8 courses. Cross over patients whose diseases progress after 2 courses of either Arm I or Arm II or who fail to respond after 3 courses to the other Arm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; PRED - 5, 20, and 50 mg tablets; VCR - 1 and 5 mg ampules, ADR - 10 mg vials; CTX - 100, 200, and 500 mg vials.

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 00761078

8.0025 PHASE III STUDY OF RADIOTHERAPY WITH OR WITHOUT CHOP (CTX/ADR/VCR/PRED) CHEMOTHERAPY FOR NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) SWOG-7433; MDAR-116

OBJECTIVES:

I. Compare the efficiency of extended-field radiotherapy plus CHOP (cyclophosphamide/adriamycin/vincristine/prednisone) combination chemotherapy vs. radiotherapy alone in patients with non-Hodgkin's lymphoma.

PROTOCOL ENTRY CRITERIA: Previously untreated patients between 15 and 65 years of age with newly diagnosed non-Hodgkin's lymphoma, Stages I, IE, II or IIE (Ann Arbor Clinical Staging Criteria). Exploratory laparotomy must be done on all patients unless Stage IV involvement has been demonstrated. Disease must be classified according to the criteria of Rappaport and in accordance with the SWOG lymphoma cell type code. Patients with diffuse lymphoma above the diaphragm may be entered without a staging laparotomy (Reported February 1978).

PROTOCOL OUTLINE: Randomized study.

3 groups of lymphoma patients will be treated: Group I - all histological types with disease above diaphragm; Group II - nodular type with disease below diaphragm; Group III - diffuse histological type with disease below diaphragm. Groups I and II are randomized to Arm I or Arm II. Group III patients are registered on study and entered to Arm II only.

Arm I: Radiotherapy. 2 MeV Cobalt-60 teletherapy. Treatment of supradiaphragmatic mantle or abdominal fields is modified according to site and extent of disease.

Arm II: Radiotherapy plus 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; and Prednisone, PRED, NSC-10023.

STRATIFICATION BY: Participating institutions, lymphoma cell type, extent of disease, site of disease.

SPECIAL STUDY PARAMETERS: Serum protein electrophoresis, lymphangiogram, bone-marrow core biopsy, whole-lung tomograms, exploratory laparotomy and splenectomy.

END POINTS: Response/remission rate, remission duration, survival rate, objective tumor response.

CURRENT STATUS: 298 patients (152 in Group I and 146 in Group II) will be entered.

DOSAGE SCHEDULE:

Arm I: Group I patients receive Radiotherapy to supra-mediastinal mantle - 4000 rads given over 4 weeks (200 rads/day 5 days/week) to opposing anterior and posterior superdiaphragmatic fields. Include thyroid, shield larynx, humoral heads, cervical region of spinal cord, and entire spinal cord after 2000 rads have been given. For mediastinal involvement, extend Radiotherapy to the full mantle. For high cervical node involvement, include Waldeyer's ring in 2 lateral, opposing trapezoidal fields. Group II and III patients receive Radiotherapy to whole abdomen - 3000 rads/day 5 days/week to entire abdomen from the dome of the diaphragm to the pelvis. Give supplementary dose to ensure femoral node dose of 3000 rads. Use shielding to maintain a total dose of 2400 rads to the liver, 2000 rads to the kidneys. For patients with disease limited to the inguinal nodes, give Radiotherapy to pelvis only.

Arm II: Four to six weeks following Radiotherapy (as in Arm I), Group I and II patients begin Chemotherapy. Group III patients receive Chemotherapy followed by Radiotherapy (as in Arm I). CHOP: CTX - 600 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 1; VCR - 1.4 mg/sqm iv on day 1 (maximum single dose 2 mg); PRED - 100 mg/day po on days 1 through 5. Repeat course q 21 days for a total of 6 courses. Delay course if necessary for hematological toxicity.

Remove from study all patients who do not achieve complete remission at the completion of their treatment. Follow up all complete responders to compare 2-year-disease-free interval rate. Document all relapses by biopsy if possible.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; PRED - 5 and 50 mg tablets; VCR - 1 mg vials; CTX - 100 and 500 mg vials.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 01160279

8.0026 PHASE III COP VS CHOP CHEMOTHERAPY PLUS LEV & BCG IMMUNOTHERAPY & LEV MAINTENANCE FOR STAGES III & IV NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) SWOG-7713/14

OBJECTIVES:

I. Compare the effectiveness, in terms of response rate, of two chemoimmunotherapy regimens (CHOP: cyclophosphamide/adriamycin/vincristine/prednisone plus levamisole (LEV) vs. LEV plus BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma.

II. Compare the duration of documented complete response obtained by continued maintenance immunotherapy with LEV vs. no maintenance therapy for complete responders to induction therapy.

III. Estimate the complete response rate obtained by continued chemoimmunotherapy with COP: CTX/VCR/PRED plus LEV for patients with impaired cardiac function (not eligible for treatment with adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with CHOP-LEV with or without BCG.

IV. Estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used.

V. Continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases.

VI. Establish baseline and serial data on immunologic status in both chemoimmunotherapy groups.

PROTOCOL ENTRY CRITERIA: Patients with advanced non-Hodgkin's lymphoma, any histologic type, or with mycosis fungoides, without prior chemotherapy, or in relapse following radiotherapy. Previously untreated patients must be carefully staged and must be Ann Arbor Stages III, IIIE, or IV. Patients with CSII diffuse lymphoma (and if below the diaphragm, those who refuse laparotomy) are eligible (Amendment 1, June 1978).

PROTOCOL OUTLINE: Randomized study. Enter patients with mycosis fungoides or impaired cardiac status to Arm IV.

Induction.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Arm II: 3-Drug Combination Chemotherapy, Hormone Therapy, plus Immunotherapy. CHOP, as in Arm I, plus Levamisole, LEV, NSC-177023.

Arm III: 3-Drug Combination Chemotherapy, Hormone Therapy, plus Immunotherapy. CHOP plus LEV, as in Arm II, plus BCG-Pasteur, BCG, NSC-B116328.

Arm IV: 2-Drug Combination Chemotherapy, Hormone Therapy, plus Immunotherapy. COP: CTX, VCR, PRED, plus LEV.

Maintenance.

Arm V: No further therapy.

Arm VI: Immunotherapy. LEV.

CNS Prophylaxis: Enter all patients with diffuse or nodular histiocytic lymphoma. Single-agent Intrathecal Chemotherapy. Cytosine arabinoside, ARA-C, NSC-63878.

STRATIFICATION BY: Participating institutions; nodular vs. diffuse histologies; adequate vs. impaired bone marrow reserves; presence vs. absence of bone marrow involvement; performance status: 1 vs. 2, 3, or 4.

SPECIAL STUDY PARAMETERS: CSF analysis, bone marrow biopsy, lymphangiogram, skin tests, quantitative immunoglobulins.

END POINTS: Response/remission rate, response duration, CNS relapse rate, survival time, immunocompetence.

CURRENT STATUS: About 500 patients will be entered in about 20 months.

DOSAGE SCHEDULE:

Induction.

Arm I: CHOP: On day 1 give CTX - 750 mg/sqm (400 mg/sqm for patients with impaired bone marrow reserve - IBMR) iv; ADR - 5 mg/sqm (25 for IBMR) iv; VCR - 1.4 mg/sqm (maximum dose - 2 mg); PRED - 100 mg po on days 1 through 5. Repeat course q 3 weeks for 8 courses.

Arm II: CHOP, as in Arm I, plus LEV - 100 mg/sqm po on days 6, 7, 13, and 14 of each course.

Arm III: CHOP, plus LEV as in Arm II, plus BCG - 2-10 x 10 to the 8th organisms on days 8 and 15 of each course by scarification to the rotating sites on upper and lower extremities.

Evaluate all patients in Arms I, II, and III and enter partial responders (PR) to Arm IV. Carefully restage all complete responders, if occult or residual disease is found, give 3 more courses of Induction Therapy (maximum cumulative ADR dose 550 mg/sqm, 450 if prior mediastinal radiotherapy), then enter PR to Arm IV.

Arm IV: COP: CTX - 200 mg/sqm po on days 1 through 5; VCR - 1.4 mg/sqm iv on day 1; PRED - as in Arm I; plus LEV - 100 mg/sqm po in divided doses on days 15 and 16. Repeat course q 28 days for 8 courses, then restage CR.

Maintenance.

Arm V: No Immunotherapy.

Arm VI: LEV - 100 mg/sqm po for 2 days q 2 weeks for a total of 18 months.

CNS Prophylaxis: ARA-C - 100 mg it before Induction Therapy, and after 4 and 8 courses.

Drug modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg ampules; ADR - 10 mg ampules; BCG - 6 plus or minus 4 times 10 to the 8th viable organisms per vial; LEV - 50 mg tablets; ARA-C - 100 mg vials.

DATE SUMMARIZED: 04/79

PATIENT ACCRUAL: 03230279

8.0027 PHASE III INDUCTION WITH ACOP, CNS THERAPY, & MAINTENANCE WITH ACOP/6-MP/MTX (IV & IT)/HC FOR CHILDHOOD NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) SWOG-7905; MDAR-356

OBJECTIVES:

I. Determine the effectiveness of Induction with combination chemotherapy ACOP: vincristine/adriamycin/cyclophosphamide plus prednisone, followed by CNS therapy with intrathecal (it) methotrexate/hydrocortisone plus radiotherapy, followed by Maintenance with combination chemotherapy ACOP plus 6-mercaptopurine (6-MP)/methotrexate (MTX-iv and it)/hydrocortisone (HC).

II. Compare effect of above regimen with that of protocol SWOG-76152, a modified LSA-2-L-2 regimen.

PROTOCOL ENTRY CRITERIA: Newly diagnosed, untreated patients under 21 years of age with biopsy-confirmed non-Hodgkin's lymphoma.

PROTOCOL OUTLINE: Nonrandomized study. Prior to study entry randomize eligible patients to this study or to SWOG-7615 in a ratio of 3:1. Enter all patients with untreated diffuse undifferentiated Burkitt's lymphoma or B cell leukemia to this study without randomization.

Induction:

3-Drug Combination Chemotherapy plus Hormone Therapy. ACOP: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; plus Prednisone, PRED, NSC-10023.

CNS-Therapy: 2-Drug Intrathecal Chemotherapy. Methotrexate-IT, MTX-IT, NSC-740; Hydrocortisone, HC, NSC-10483. Radiotherapy, Cobalt-60, 2 MEV or higher energy to primary mass, gross residual disease and cranium.

Maintenance:

6-Drug Combination Chemotherapy plus Hormone Therapy. ACOP plus MTX; 6-Mercaptopurine, 6-MP, NSC-755; HC.

STRATIFICATION: Participating institutions; histologic type: convoluted vs. histocytic vs. undifferentiated.

SPECIAL STUDY PARAMETERS: Kidney and liver function; bone marrow aspirate and biopsy; CSF cell count and protein level; bone and CAT scans; IVP; liver, spleen and node measurements.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 90 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Induction:

ACOP: VCR - 1.5 mg/sgm (maximum 2 mg) iv push on days 1, 8, 15, 22 and 29; ADR - 60 mg/sqm iv push or infusion on day 1; CTS - 800 mg/sqm rapid iv infusion on day 15; PRED - 40 mg/sqm/day (maximum 60 mg) po in 3 or 4 divided doses on days 2 through 28 tapering off over 7 days thereafter; premedication hydration and allopurinol. Intrathecal CNS therapy: Given on days 22 through 39, and on days 36 through 53 for patients with large abdominal or mediastinal mass. Administer simultaneously with systemic therapy for patients with CNS involvement at time of diagnosis. MTX - 12 mg/sqm (maximum 15 mg) it biweekly for 5 doses; HC - 12 mg/sqm it given with MTX biweekly for 5 doses, followed by 1 ml Elliott's B solution. Give one additional dose on day 29 to patients with CNS involvement, and continue it therapy in these patients until CNS is free of blasts on 2 examinations. Radiotherapy: Beginning on day 16 give 3000 rads in 4 weeks to the site of the primary tumor to Stage I and II patients, to the primary tumor and to gross residual disease to Stage III and IV patients. Omit Radiotherapy to patients with massive disseminated disease. Cranial Radiotherapy: Beginning on day 22 give 2400 rads in 2.5 weeks to the whole brain and to the cervical spine to C2.

Maintenance:

Begin on day 43 provided that the absolute granulocyte count is above 1000. VCR - 1.5 mg/sqm iv push on days 1 and 15 in the first year, on day 1 only in the second year; CTX - 800 mg/sqm iv on day 15 q 6 weeks in the first year, on day 1 q 6 weeks in the second year; ADR - 60 mg/sqm iv on day 1 q 6 weeks until a total dose of 500 mg/sqm (360 mg/sqm if mediastinum is being irradiated) is reached; MTX - 60 mg/sqm iv push or im q 6 weeks starting on day 71 (leucovorin rescue: CF - 9 mg po 24 to 36 hrs if necessary later); 6-MP - 75 mg/sqm/day po on days 71 through 85; MTX - 15 mg/sqm it 2 months for 5 doses starting on day 85; HC - 12 mg/sqm it following each dose of MTX-IT; PRED - 40 mg/sqm/day in 3 or 4 divided doses on days 14 through 28. Repeat course q 6 weeks until maximum ADR dose is reached, then continue 6-MP for 2 more weeks (4 weeks total) and give VCR on day 1 only. Continue therapy q 6 weeks for 2 years from diagnosis for Stages I, II, and III, and for 3 years for Stage IV disease. Remove from study patients who do not achieve complete remission after the first 6-week course of Maintenance therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CTX - 200 and 500 mg vials; PRED - 5, 10 and 20 mg tablets; ADR - 10 and 50 mg vials; MTX - 5 and 50 mg vials; 6-MP - 50 mg tablets; HC - 50 mg vials.

DATE SUMMARIZED: 10/79

8.0028 PHASE III CHEMOTHERAPY WITH CAVP (CTX/ADR/VCR/PRED) VS CVP (CTX/VCR/PRED) FOR DISSEMINATED NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) BCRP-7312A

OBJECTIVES:

I. Determine whether CAVP (cyclophosphamide/adriamycin/vincristine/prednisone) is more efficacious than CVP (cyclophosphamide/vincristine/prednisone) for remission induction in patients with disseminated non-Hodgkin's lymphomas.

II. Evaluate the efficacy of Maintenance chemotherapy in prolonging both remission duration and survival in those patients who achieve CR after induction therapy.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven non-Hodgkin's lymphoma who have at least Stage III disease clinically and who are previously untreated or have received only localized radiotherapy. Patients may not be candidates for laminar air flow housing during chemotherapy for Stage III or IV diffuse histiocytic lymphoma.

PROTOCOL OUTLINE: Randomized study for Induction and Maintenance.

Induction.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. CAVP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. CVP: CTX; VCR; PRED.

Consolidation. Enter CR from Arms I and II.

2-Drug Combination Chemotherapy plus Hormone Therapy. CCNU, NSC-79037; Bleomycin, BLEO, NSC-125066; PRED.

Maintenance. Randomize CR after Consolidation to Arm III or Arm IV.

Arm III: No further therapy.

Arm IV: Single-agent Chemotherapy. CTX.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, chest x-ray, pulmonary function studies, KUB.

END POINTS: Response/remission rate, duration of response, recurrence rate, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CAVP: CTX - 100 mg/sqm iv on day 1; ADR - 45 mg/sqm iv push on day 1 (total cumulative dose not to exceed 555 mg/sqm); VCR - 1.4 mg/sqm (maximum 2.0 mg) iv push on days 1 and 8; PRED - 40 mg/sqm/day po on days 1 through 10. Repeat course q 21 days.

Arm II: CVP: CTX, VCR, and PRED as in Arm I. Repeat course q 21 days.

Consolidation: CCNU - 100 mg/sqm po on day 1; BLEO - 20 mg/sqm im on days 1 and 8; PRED - 40 mg/sqm/day po on days 1 through 10. Repeat course q 21 days.

Arm III: No further treatment.

Arm IV: CTX - 1500 mg/sqm iv q month.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

8.0029 COMBINATION RADIOTHERAPY, CHEMOTHERAPY AND IMMUNOTHERAPY FOR STAGE III NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) MDA-3

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy and and radiotherapy for induction remission for Stage III lymphomas.

II. Determine if maintenance chemotherapy or immunotherapy will prolong remission duration.

III. Determine if immunotherapy with BCG or viral oncolysates enhances host immunocompetence and clinical status.

IV. Determine if the optimal duration of maintenance therapy of patients is in complete remission.

V. Determine if staging celiotomy will affect prognosis in non-Hodgkin's lymphoma.

PROTOCOL ENTRY CRITERIA: Patients with non-Hodgkin's lymphoma Stage III, IIIe or Stage II diffuse and nodular with massive intra-abdominal disease.

PROTOCOL OUTLINE: Study randomized for Maintenance only. Patients with nodular lymphoma enter Regimen A, then Regimen B. Patients with diffuse lymphoma enter Regimen C, then Regimen D. Following Induction, patients in complete remission are randomized to Arms I, II and III.

Induction:

Regimen A: 5-Drug Combination Chemotherapy. Reduced-dose CHOP plus Bleomycin. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; plus Bleomycin, BLEO, NSC-125066.

Regimen B: Radiotherapy. Irradiation of the total abdomen, head and neck, and axillae.

Regimen C: 5-Drug Combination Chemotherapy. Full dose CHOP plus Bleomycin.

Regimen D: Radiotherapy. Irradiation of limited abdominal fields, head and neck, axillae, and the mediastinum.

Maintenance:

Arm I: 3-Drug Combination Chemotherapy. CTX; VCR; PRED.

Arm II: 2-Agent Immunotherapy. BCG-unspecified, No NSC number; plus Lymphoma oncolysate vaccination.

Arm III: No further treatment.

STRATIFICATION BY: Disease type (nodular or diffuse lymphoma), age (less than 40 years or more than 40 years).

SPECIAL STUDY PARAMETERS: Pulmonary function tests, arterial gases, liver and renal function tests, ECG, skin tests (dermatophytin, varidase, mumps, PPD), liver and spleen scans, protein electrophoresis, in vitro lymphocyte cytotoxicity studies, in vitro complement-dependent cytotoxicity assay.

END POINTS: Response/remission rate; duration of remission, duration of survival, morbidity/toxicity of treatment.

CURRENT STATUS: About 120 patients will be entered.

DOSAGE SCHEDULE:

Induction:

Regimen A: ADR - 35 mg/sqm iv on day 1; CTX - 600 mg/sqm iv on day 1; VCR - 1.4 mg/sqm iv on day 1; BLEO - 5 mg/sqm iv on day 1; PRED - 40 mg/sqm po daily on days 1 through 5. Repeat course q 3 to 4 weeks. Continue treatment for 12 to 18 months.

Regimen B: Co-60 Source - 3000 rads total abdominal dose over 4 weeks or split course Radiotherapy to upper two-thirds of abdomen, followed by rest period of 4 to 8 weeks and then irradiation of the pelvic region; plus 4000 rads to the head and neck over 4 weeks. Radiotherapy begins after hematological recovery from Regimen A Chemotherapy.

Regimen C: ADR - 50 mg/sqm iv on day 1; BLEO - 5 mg/sqm iv on day 1; CTX - 750 mg/sqm iv on day 1; VCR - 1.4 mg/sqm iv on day 1; PRED - 40 mg/sqm po on days 1 through 5. Repeat course q 3 to 4 weeks.

Regimen D: Co-60 source - 3000 rads to limited abdominal fields (primary site of massive abdominal disease). Administer additional 1000 to 2000 rads to residual disease; plus 4000 rads to involved regions of the head and neck and mediastinum over 4 weeks. Begin Radiotherapy after recovery from toxic effects of Regimen C Chemotherapy.

Maintenance:

Arm I: CTX - 600 mg/sqm iv on day 1; VCR - 1.4 mg/sqm iv on day 1; PRED - 40 mg/sqm po on days 1 through 5. Repeat course in 4 weeks. Treat patients for 12 months.

Arm II: Patients receive either BCG scarification or lymphoma oncolysate vaccination at 2-week intervals for 18 weeks (9 applications). Patients then cross over to receive the other immunotherapeutic agent for the next 18 weeks. Thereafter patients receive BCG one week and lymphoma oncolysate vaccination the next week for 12 months of alternating Immunotherapy.

Arm III: No further treatment. Continue followup.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/76

8.0030 CHOP PLUS LATE INTENSIFICATION WITH COAP-BLEO, AND ALTERNATE THERAPIES FOR NONRESPONDING PATIENTS WITH NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) MDAR-215; MDA-DT-7704

OBJECTIVES:

I. Determine whether alternate combination chemotherapies with HOAP-BLEO (ADR/ARA-C/VCR/PRED/BLEO) and intensification with IPP/MTX/VP-16 will improve the complete response (CR) rate in patients with diffuse non-Hodgkin's lymphoma not or only partially responding to CHOP(CTX/ADR/VCR/PRED).

II. Determine the efficacy of alternate therapy with NM/VCR/PCB/PRED/BLEO for patients with nodular non-Hodgkin's lymphoma not responding to CHOP.

III. Determine the efficacy of late intensification with COAP-BLEO (CTX/VCR/ARA-C/PRED/BLEO) for CR patients following CHOP induction.

PROTOCOL ENTRY CRITERIA: Adult patients with measurable lesions of biopsy proven non-Hodgkin's lymphoma, all types in stages II, III or IV, who have not had over 2 weeks of treatment with any of the protocol drugs. Patients must have a normal EKG, and if on extensive radiotherapy must have their doses decreased by 20%.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Enter all patients. 3-Drug Combination Chemotherapy plus Hormone Therapy, followed, for late intensification for CR, by 4-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; COAP-BLEO: CTX; VCR; ARA-C; PRED; BLEO.

Regimen B: Enter patients with diffuse histology, not in CR following Regimen A. 4-Drug Combination Chemotherapy plus Hormone Therapy. HOAP/BLEO: ADR; Cytosine arabinoside, ARA-C, NSC-63878; VCR; PRED; Bleomycin, BLEO, NSC-125066; followed, for late intensification for CR, by 3-Drug Combination Chemotherapy. Isophosphamide, IPP, NSC-109724; Methotrexate, MTX, NSC-740; VP-16213, VP-16, NSC-141540.

Regimen C: Enter patients with nodular histologies not in CR following Regimen A. 4-Drug Combination Chemotherapy plus Hormone Therapy. Nitrogen Mustard, NM, NSC-762; VCR; Procarbazine, PCB, NSC-77213; PRED; BLEO.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, objective tumor response, duration of remission, survival.

CURRENT STATUS: About 150 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Regimen A: CTX - 750 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; VCR - 1.4 mg/sqm (maximum 2 mg) iv on days 1 and 5; PRED - 100 mg/day po for 5 days. Enter CR to CTX - 100 mg/sqm/day iv or po on days 1 through 5; VCR - 1.4 mg/sqm iv single dose; ARA-C - 100 mg/sqm iv or sc on days 1 through 5; PRED - 100 mg po on days 1 through 5; BLEO - 15 units iv or im on days 1 and 5.

Regimen B: ADR - 40 mg/sqm iv on day 1; ARA-C - 70 mg/sqm iv on days 1 through 5; VCR - 1.4 mg/sqm iv on days 1 and 5; PRED - 100 mg on days 1 through 5; BLEO - 15 units/day iv or im on days 1 and 5. Enter CR to IPP - 1000 mg/sqm; MTX-30 mg/sqm iv or im on days 3 and 14; VP-16 - 75 mg/sqm iv on days 1 through 5.

Regimen C: NM - 8 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm iv on day 1; PCB - 100 mg/sqm/day on days 1 through 14; PRED - 15 mg on days 1 through 10; BLEO - 15 units iv or im on days 1 and 8.

Length of courses or total treatment periods are not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

8.0031 CHEMOTHERAPY WITH CHOP-BLEO PLUS MAINTENANCE WITH OAP IN PEPA PROGRAM FOR DIFFUSE HISTIOCYTIC LYMPHOMA

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PROTOCOL NUMBER(S) MDAR-260; MDA-DT-7806

OBJECTIVES: (This protocol replaces MDAR-27.)

I. Determine whether higher doses of chemotherapy with CHOP-BLEO: cyclophosphamide (CTX), adriamycin (ADR), vincristine (VCR), prednisone (PRED) and bleomycin (BLEO) administered in the Protected Environment Prophylactic Antibiotic (PEPA) Program will produce the optimum complete remission rate and longer disease-free survival.

PROTOCOL ENTRY CRITERIA: Patients 15 to 65 years old with measurable, biopsy-confirmed diffuse histiocytic lymphoma Stage III or IV without prior chemotherapy or CNS disease at diagnosis, and with adequate cardiac status.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: Enter all patients 48 hours after onset of antibiotic therapy to PEPA, plus 4-Drug Combination Chemotherapy plus Hormone Therapy. CHOP-BLEO: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; Bleomycin, BLEO, NSC-125066.

Maintenance: 2-Drug Combination Chemotherapy plus Hormone Therapy. OAP: VCR; Cytosine arabinoside, ARA-C, NSC-63878; PRED.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response remission rate, toxicity/morbidity of treatment, disease-free interval, survival time.

CURRENT STATUS: About 40 patients will be entered in about 4 years.

DOSAGE SCHEDULE:

Induction: CTX - 1200 mg/sqm iv on day 1; 2nd course: 1500 mg/sqm; 3rd course: 1800 mg/sqm; 4th through 6th courses: 750 mg/sqm; ADR - 75 mg/sqm iv on day 1; 2nd course: 90 mg/sqm; 3rd course: 110 mg/sqm; 4th through 6th courses: 50 mg/sqm; VCR - 1.0 mg/sqm iv (maximum dose 1.5 mg) on days 1 and 5 for 6 courses; PRED - 25 mg/day po days 1 through 5 for 6 courses; BLEO - 5.0 mg iv 6 hours after VCR; courses 2 through 6: 15 mg.

Repeat courses 1, 2, and 3 upon patient's recovery from toxicity of previous course. Give courses 4, 5 and 6 q 3 to 4 weeks after recovery from myelosuppression.

Maintenance: OAP: VCR - 1.0 mg/sqm iv (maximum dose 1.5 mg) on day 1; ARA-C - 100 mg/sqm sc in 4 divided doses on days 1 through 5; PRED - 25 mg/day po on days 1 through 5. Continue Maintenance therapy q 3 weeks for 1 year.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

8.0032 PHASE II CHEMOTHERAPY WITH AMSA FOR NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) MDAR-288; MDA-DT-7842

OBJECTIVES:

I. Determine the efficacy of AMSA as a second line treatment for non-Hodgkin's malignant lymphoma.

II. Further study the toxicity of AMSA.

PROTOCOL ENTRY CRITERIA: Patients with measurable lesions of non-Hodgkin's lymphoma, who have failed to respond to chemotherapy and are not eligible for higher priority protocols. Patients must have been off all chemotherapy and radiotherapy for at least 3 weeks and have adequate bone marrow function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

AMSA - 40 mg/sqm iv on days 1 through 3 q 3 weeks. Reduce dosage to 30 mg/sqm in cases of liver dysfunction or extensive prior radiation. Continue therapy for responders with 20% adjustments in dose to achieve adequate myelosuppression (granulocyte count nadir about 500/cumm). Remove from study patients without benefit after 2 courses or those with unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 00190579

8.0033 RADIOTHERAPY, CHEMOTHERAPY WITH CHOP-BLEO, AND IMMUNOTHERAPY FOR STAGE III NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) MDAR-5

OBJECTIVES:

I. Determine whether staging celiotomy will affect prognosis in non-Hodgkin's lymphoma patients.

II. Determine whether intensive combination chemotherapy and radiotherapy will improve remission Induction rates and prolong survival.

III. Determine whether immunotherapy will prolong remission duration.

IV. Compare survival time and remission duration with comparable groups of recent historical control patients.

PROTOCOL ENTRY CRITERIA: Laparotomy-staged III, IIIE non-Hodgkin's lymphoma, including Stage II diffuse lymphoma with massive intra-abdominal disease with histiocytic, mixed or poorly differentiated lymphocytic cell types. Patients are preferably 65 years old and may not have had prior therapy.

PROTOCOL OUTLINE: Enter patients with nodular lymphoma successively to Regimen A, Regimen B, and Regimen C, repeating Regimen A before and after Regimen C. Enter patients with diffuse lymphoma successively to Regimen D, Regimen B (except patients with minimal abdominal disease), and Regimen C, repeating Regimen A before and after Regimen C. Following this therapy, patients with nodular or diffuse disease who are in complete remission are randomized to Arms I and II.

Regimen A: 4-Drug Combination Chemotherapy plus Hormone Therapy. Reduced dose regimen. CHOP plus BLEO: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066; Prednisone, PRED, NSC-10023.

Regimen B: Radiotherapy to abdomen.

Regimen C: Radiotherapy to neck and/or axilla.

Regimen D: 4-Drug Combination Chemotherapy plus Hormone Therapy. Full-dose regimen. CHOP plus BLEO: CTX, ADR, VCR, BLEO, and PRED.

Arm I: Immunotherapy.

Arm II: No Immunotherapy.

STRATIFICATION BY: Histological type, nodular vs. diffuse disease, extent of tumor spread.

SPECIAL STUDY PARAMETERS: Laparotomy staging.

END POINTS: Response/remission rate, remission duration, survival time, survival rate.

CURRENT STATUS: Approximately 20 patients will be entered each year.

DOSAGE SCHEDULE:

Regimen A: CTX - 600 mg/sqm iv on day 1. ADR - 35 mg/sqm (total maximal cumulative dose - 450 mg/sqm) iv on day 1. VCR - 1.4 mg/sqm (total dose/injection not to exceed 2 mg) iv on day 1. BLEO - 5 units/sqm (total maximal cumulative dose - 200 mg) iv on day 1. PRED - dose not given. Repeat course once after 3-4 weeks depending on wbc and platelet count. Following hematological recovery after the second course of Chemotherapy, enter patients to Regimen B Radiotherapy.

Regimen B: Total abdominal Radiotherapy. Administer 750 rads q week for a total tumor dose of 3000 rads given over a period of 4 weeks. Repeat Regimen A Chemotherapy for 2 courses. After hematological recovery, enter patients to Regimen C Radiotherapy.

Regimen C: Radiotherapy to peripheral regions. Administer a total tumor dose of 4000 rads over a period of 4 weeks to head and neck region and/or axilla. Repeat Regimen A Chemotherapy for 6 courses.

Regimen D: CTX - 750 mg/sqm iv on day 1. ADR - 50 mg/sqm iv on day 1. VCR - 1.4 mg/sqm iv on day 1. BLEO - 5 units/sqm iv on day 1. PRED - 40 mg/sqm po on days 1 through 5. Repeat course q 3 or 4 weeks, depending on hematological status, for a total of 4 courses. Enter patients with measurable or massive abdominal disease to Regimen B Radiotherapy, followed by 4 additional courses of Regimen D Chemotherapy, followed by Regimen C Radiotherapy. Additional Radiotherapy of 500 to 1000 rads may be given for residual disease to very reduced fields. Repeat Regimen D Chemotherapy for 8 additional courses. Repeat Regimen D Chemotherapy. For patients with minimal abdominal disease, omit Regimen B Radiotherapy. Following 4 courses of initial Regimen D Chemotherapy, administer Regimen C Radiotherapy, followed by 8 additional courses of Regimen D Chemotherapy.

Closely monitor all patients with nodular or diffuse lymphoma for toxicities due to ADR and BLEO. Discontinue these agents when maximum cumulative dose has been given. Restage all patients upon completion of appropriate regimens and randomize all patients in complete remission to Arms I and II.

Arm I: Immunotherapy over a period of 12 months. No details given.

Arm II: No Immunotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/79

8.0034 RADIOTHERAPY, CHEMOTHERAPY WITH CTX/ADR/VCR/BLEO, HORMONE THERAPY WITH PRED, & BCG IMMUNOTHERAPY FOR STAGES I & II NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) MDAR-84

OBJECTIVES:

I. Determine whether staging celiotomy will affect prognosis for non-Hodgkin's lymphoma patients.

II. Determine whether chemotherapy and/or immunotherapy will prolong remission duration.

III. Determine whether immunotherapy with BCG scarification and/or viral oncolysate can enhance the immunocompetence of lymphoma patients and correlate such changes with clinical status.

IV. Determine the optimal duration of Maintenance therapy for Stages I, II lymphoma after achieving complete remission status.

PROTOCOL ENTRY CRITERIA: Previously untreated patients less than 70 years of age with histologically proven non-Hodgkin's lymphoma Stages I, II, Ie or IIe after staging celiotomy.

PROTOCOL OUTLINE: Study randomized for Maintenance. All patients in complete remission following Induction are randomized to Arms I, II, or III.

Induction: Radiotherapy. Co-60 or megavoltage irradiation.

Maintenance:

Arm I: 4-Drug Combination Chemotherapy and Hormone Therapy. CHOP plus BLEO: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; Bleomycin, BLEO, NSC-125066.

Arm II: 2-Agent Immunotherapy. BCG, type not specified; plus lymphoma viral oncolysate.

Arm III: Control. No further therapy.

STRATIFICATION BY: Participating institution; disease stage.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate; toxicity/morbidity of treatment; survival time; survival rate; remission duration; changes in immunocompetence.

CURRENT STATUS: Approximately 30 patients will be entered each year; 40 patients are required in each randomization arm for evaluation.

DOSAGE SCHEDULE:

Induction: Radiotherapy to tumor sites. 4000 rads to involved regions of head, neck and/or axilla over a period of 4 weeks, for patients with diffuse lymphoma and high cervical node involvement, 3000 rads prophylactic Radiotherapy to Waldeyer's ring given over a period of 4 weeks. For patients with mediastinal disease, 4000 rads given to the upper mediastinum or 2500 to 3000 rads given to the lower mediastinum. Radiotherapy to total abdomen. 3000 rads given over a period of 4 weeks through parallel, opposing anterior and posterior fields plus 1000 rads additional tumor dose through reduced fields for residual disease.

Maintenance:

Arm I: CHOP plus BLEO: CTX - 750 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; VCR - 1.4 mg/sqm iv on day 1; PRED - 40 mg/sqm po on days 1 through 5; BLEO - 5 mg/sqm iv on day 1. Repeat course q 28 days for a total of 12 months.

Arm II: BCG by scarification followed by lymphoma viral oncolysate vaccination at 2-week intervals, for a total of 12 months.

Arm III: No further therapy.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/76

8.0035 COMBINATION THERAPY WITH THIO-TEPA/VCR/CLB/PRED/RADIOTHERAPY PLUS CTX/ADR/L-PAM/PRED WITH/WITHOUT MBV IMMUNOTHERAPY FOR NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) MSKCC-7676

OBJECTIVES:

I. Increase survival of patients with good-risk non-Hodgkin's lymphoma by the use of a moderately intensive combined chemotherapy-radiotherapy regimen suitable for out-patients.

II. Test the efficacy of mixed bacterial vaccines (MBV) in prolonging remission and survival.

PROTOCOL ENTRY CRITERIA: Patients with non-Hodgkin's lymphoma of favorable histology, including all modular lymphomas and diffuse well-differentiated lymphomas. Patients must be previously untreated or have had only minimal prior therapy.

PROTOCOL OUTLINE: Regimen A only is randomized.

Regimen A:

Arm I: Immunotherapy. Mixed bacterial vaccine, MBV.

Arm II: No Immunotherapy.

Regimen B: 3-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. Thio-tepa, NSC-6396; Vincristine, VCR, NSC-67574; Chlorambucil, CLB, NSC-3088; plus Prednisone, PRED, NSC-10023; plus Radiotherapy to involved field.

Regimen C: 3-Drug Combination Chemotherapy plus Hormone Therapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Melphalan, L-PAM, NSC-8806; plus PRED.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Sedimentation rate, bone marrow aspirate and biopsy, lymphangiogram, quantitative immunoglobulins and immunoelectrophoresis, screening profile, skin tests for recall antigens, immunologic markers, cytokinetic parameters, electron microscopy.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival, cutaneous reactivity.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A:

Arm I: Initiate 12 to 5 days prior to Chemotherapy: MBV - 0.1 ml x 10 to the minus 3 sc initial dose. Increase 3-fold daily until desired level of local and systemic reactions is achieved. Then administer a single dose at the desired level, repeating 5 days prior to each cycle of Chemotherapy. Discontinue vaccine upon completion of Chemotherapy.

Arm II: No Immunotherapy.

Regimen B: Thio-tepa - 0.8 mg/kg (30 mg/sqm) iv on day 1; VCR - 1.4 mg/sqm (maximum 2 mg) on day 1; CLB - 0.13 mg/kg/day (5 mg/sqm) for 10 to 14 days, depending on blood counts; PRED - 40 mg/sqm/day on days 1 through 7. Repeat course on day 23 and q 3 weeks thereafter. Continue for 6 months after complete remission is attained, then proceed to Regimen C. Enter patients failing to achieve a complete remission after 6 months of therapy to another 6-month course in Regimen B. Enter patients to Radiotherapy, timing dependent upon patient's response to Chemotherapy-3000 to 3500 rads to involved fields given in 3.5 to 4 weeks to all sites of initially bulky disease, or give about 2000 rads if total modal irradiation is required. Enter responders to Radiotherapy during the first six months of Regimen B Chemotherapy after complete response. If partial remission is obtained after 6 months in Regimen B, give Radiotherapy to residual disease while repeating Regimen B Chemotherapy for 6 more months.

Regimen C: Initiate after a 4-week rest following Radiotherapy and 2 to 3 weeks following completion of the Regimen B Chemotherapy: CTX - 600 mg/sqm iv on day 1; ADR - 25 mg/sqm iv on day 1; L-PAM - 6 mg/sqm/day po on days 1 through 4; plus PRED - 60 mg/sqm/day po on days 1 through 5. Repeat q 21 to 28 days for a total of 4 courses. Consider treating on another regimen patients who relapse or who after 3 courses fail to achieve a complete remission.

Dosage modificiations for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/78

8.0036 CHOP (CTX/ADR/VCR/PRED) VS BLEO-CHOP CHEMOTHERAPY FOR ADVANCED STAGES OF DIFFUSE B-CELL LYMPHOMA

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PROTOCOL NUMBER(S) MSKCC-7920

OBJECTIVES:

I. Compare the rate and duration of CR and PR of CHOP (cyclophosphamide/adriamycin/vincristine/prednisone) vs. bleomycin-CHOP in patients with diffuse B-cell lymphoma (histiocytic, mixed, and lymphocytic poorly differentiated types).

PROTOCOL ENTRY CRITERIA: Patients with Stages III/IV B-cell type malignant lymphomas of the diffuse histiocytic, mixed histiocytic-lymphocytic, and lymphocytic poorly differentiated varieties. Patients with lymphoblastic, undifferentiated and Burkitt's lymphomas will not be entered. Patients must not be over 65 years of age. Emphasis will be placed upon those who have had minimal or no prior therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Arm II: 4-Drug Combination Chemotherapy plus Hormone Therapy, alternating with 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP plus Bleomycin, BLEO, NSC-125066, alternating with CHOP alone. Intrathecal prophylaxis with Methotrexate, MTX, NSC-740, in patients with bone marrow involvement.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests, bone marrow aspiration and biopsy, chemical profile, chest x-ray, lymphangiogram, gallium scan, serum immunoelectrophoresis, creatinine clearance, pulmonary function test, IVP, liver and spleen scan, liver biopsy, spinal tap, lymphocyte cell markers, terminal deoxynucleotidyl transferase.

END POINTS: Response/remission rate.

CURRENT STATUS: 80 patients will be entered.

DOSAGE SCHEDULE:

Arm I: CHOP: CTX - 700 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; VCR - 1.4 mg/sqm iv on day 1; PRED - 60 mg/sqm po on days 1 through 5. Repeat every 21-28 days, according to bone marrow tolerance, for 8 cycles.

Arm II: For cycles 1 and 5: BLEO - 20 mg/sqm iv infusion for 24 hours on days 1 through 7; CHOP as in Arm I on day 8. For cycles 2, 3, 4, 6, 7, and 8: CHOP as in Arm I. Repeat cycles every 21-28 days according to bone marrow tolerance.

For patients with massive tumor burdens with manifestation of tumor lysis syndrome, give diuresis of 150 ml/hour by iv hydration and mannitol and/or Lasix diuresis. For patients with bone marrow involvement give MTX - 6.5 mg/sqm it on days 1 and 8 by lumbar puncture during cycles 2, 4, 6, and 8.

Upon completion of 8 cycles of therapy, patients will be randomized for an immune stimulant (details not given) or will go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

8.0037 CHOP (CTX/ADR/VCR/PRED) PLUS MTX PLUS IT MTX AND ARA-C WITH OR WITHOUT INITIAL SURGERY FOR CHILDHOOD NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) NCI-77-C-145; NCI-POB-7704

OBJECTIVES:

I. Study the clinical features, histology and cytology, surface markers, in vivo induction of differentiation, functional potential of tumor cells, distribution patterns of DNA and protein before and after treatment, and possible tumor markers in a group of children with non-Hodgkin's lymphoma under uniform treatment.

II. Evaluate the therapeutic effectiveness of chemotherapy with CHOP (cyclophosphamide/adriamycin/vincristine/prednisone) plus methotrexate and prophylactic intrathecal methotrexate and cytosine arabinoside with or without initial surgery in children with non-Hodgkin's lymphoma. (Intrathecal therapy added, Addendum August 1978.)

PROTOCOL ENTRY CRITERIA: Untreated patients under the age of 25 with non-Hodgkin's lymphoma and untreated patients of any age with Burkitt's lymphoma. Patients in whom all tumor has been surgically excised may be eligible, and patients with immunodeficiency syndromes and lymphoma will normally be admitted provided there is no severe disseminated infection. Patients between the ages of 10 and 25 years with mediastinal tumors and a morphological diagnosis of ALL will be included. Patients should have fresh tumor tissue available.

PROTOCOL OUTLINE: Nonrandomized study.

Surgery plus 5-Drug Combination Chemotherapy plus Hormone Therapy plus Citrovorum Rescue. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; Cytosine arabinoside, ARA-C, NSC-63878; Prednisone, PRED, NSC-10023; Citrovorum Factor, CF, NSC-3590.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hemogram, electrolytes, EKG, liver and kidney function tests, immunoglobulins, IVP, appropriate x-rays and scans, head and abdominal CAT, abdominal ultrasound, bone marrow aspiration.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Surgery - total resection of tumor whenever possible without the necessity of a mutilating procedure. Initiate Chemotherapy within days of Surgery.

Cycle 1: CTX - 1.2 g/sqm iv on day 1; MTX - 300 mg/sqm iv infusion over 1 hour followed by 60 mg/sqm/hour continuous infusion for 41 hours (begin MTX infusion on day after CTX); CF - 48 mg/sqm iv at conclusion of MTX infusion, then 12 mg/sqm iv or po q 6 hours until serum MTX is less than 5 x 10 to the minus eighth M. (MTX boost - 12.5 mg/sqm to a maximum of 12.5 mg it, 6 hours after start of MTX infusion; ARA-C - 30 mg/sqm it on days 1, 2, 3 and 7, Addendum August 1978.)

Cycles 2 and 3: Begin after marrow recovery. CHOP: CTX - 1.2 mg/sqm iv on day 1; ADR - 40 mg/sqm iv on day 1; VCR - 1.4 mg/sqm (maximum 2 mg) iv on day 1; PRED - 40 mg/sqm iv or po on days 1 through 5; MTX and CF rescue as in Cycle 1; (it MTX as in Cycle 1; ARA-C - 45 mg/sqm it on days 0, 1, and 2, Addendum August 1978).

Storage of autologous marrow will be performed at the time of recovery from Cycle 3. Marrow will be needed when patients proceed to NCI protocol 7806 (NCI-79-C-93).

Cycles 4, 5, and 6: Begin after marrow recovery. CHOP as in Cycle 2; MTX infusion and CF rescue (with it MTX boost as in Cycle 2; ARA-C - 45 mg/sqm it on day 1, Addendum August 1978).

Cycles 7-15: Treat monthly. CHOP as in Cycle 2; MTX infusion and CF rescue (with it MTX boost as in Cycle 1 but beginning on day 14, Addendum August 1978).

Patients with systemic relapse go off study and enter separate relapse protocol. Patients with CNS relapse continue treatment and receive cranial irradiation as well.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; MTX - 0.5 and 1 g vials.

DATE SUMMARIZED: 10/80

8.0038 OBSERVATION VS INTENSIVE CHEMOTHERAPY FOR NODULAR LYMPHOMAS AND DIFFUSE WELL-DIFFERENTIATED LYMPHOCYTIC LYMPHOMAS

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PROTOCOL NUMBER(S) NCI-78-C-145; NCI-MB-110

OBJECTIVES:

I. Compare observation plus palliative radiotherapy vs. intensive chemotherapy with ProMACE (cyclophosphamide/adriamycin/VP-16/prednisone/methotrexate) followed by MOPP (nitrogen mustard/vincristine/procarbazine/prednisone) in patients with nodular lymphomas and diffuse well-differentiated lymphomas.

II. Evaluate the efficacy of modified total nodal radiotherapy to consolidate CR and decrease subsequent relapses in patients with nodular poorly-differentiated lymphocytic lymphoma (NPDL), diffuse well-differentiated lymphocytic lymphoma (DWDL), diffuse intermediately well-differentiated lymphocytic lymphoma (DIDL), nodular mixed histiocytic-lymphocytic lymphoma (NML), and diffuse poorly-differentiated lymphocytic lymphoma-small cleaved cell variety (DPDL-SC).

III. Evaluate the efficacy of intensive chemotherapy for remission Induction in patients previously treated conservatively for nodular forms of lymphoma but who convert to a diffuse histology.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven DWDL, DIDL, NPDL, NML, and DPDL-SC. Patients must not have been previously treated and may not be over the age of 70. There may be no previous or coexisting malignancy except for curatively treated squamous or basal cell carcinoma of the skin or effectively treated in-situ carcinoma of the cervix.

PROTOCOL OUTLINE: Randomized study. Enter patients presenting with clinically aggressive disease (e.g., spinal cord compression, vena caval obstruction, etc.) to Arm II; randomize all others to Arms I and II.

Arm I: Observation plus Palliative Radiotherapy. Megavoltage equipment.

Arm II: Intensive Chemotherapy.

Induction: 4-Drug Combination Chemotherapy with Leucovorin Rescue plus Hormone Therapy. ProMACE: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; VP-16213, VP-16, NSC-141540; Prednisone, PRED, NSC-10023; Methotrexate, MTX, NSC-740; plus Citrovorum Factor, CF, NSC-3590.

Consolidation: 3-Drug Combination Chemotherapy plus Hormone Therapy. MOPP: Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; PRED.

Intensification: 4-Drug Combination Chemotherapy plus Hormone Therapy. ProMACE.

STRATIFICATION BY: Participating institutions, disease stage, histology.

SPECIAL STUDY PARAMETERS: Hemogram, SMAC-21, PT, PTT, protein electrophoresis, quantitative immunoglobulins, lymphangiogram, abdominal CT scan, chest x-ray, tomograms as necessary, KUB, bone marrow aspiration and biopsy with cytogenetics, EKG.

END POINTS: Response/remission rate, duration of response, relapse rate after CR, toxicity/morbidity of treatment.

CURRENT STATUS: 45 patients each will be required for Arms III and IV and 64 patients each will be required for Arms I and II.

DOSAGE SCHEDULE:

Arm I: Midplane dosages of no more than 2500 rads at the rate of 1000 rads/week. Patients with progressive disease enter Arm II.

Arm II:

Induction. ProMACE: CTX - 650 mg/sqm iv on days 1 and 8; ADR - 25 mg/sqm iv on days 1 and 8; VP-16 - 120 mg/sqm iv over 30 minutes on days 1 and 8; PRED - 60 mg/sqm/day po on days 1 through 14; MTX - 1.5 g/sqm iv over 12 hours on day 14, with adequate prehydration and concomitant hydration; CF - 50 mg/sqm iv q 6 hours for a total of 8 doses beginning 24 hours after the initiation of MTX infusion. Repeat at 28-day intervals for a minimum of 2 cycles and enter Consolidation when the rate of response to Induction begins to decrease.

Consolidation. MOPP: NM - 6 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm iv on days 1 and 8; PCB - 100 mg/sqm/day on days 1 through 14; PRED - 40 mg/sqm/day po on days 1 through 14.

Intensification. Repeat Induction therapy with identical number of cycles.

All clinical complete responders receive modified total lymphoid irradiation - 2500 rads at 750-800 rads/week.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

8.0039 COMBINATION CHEMOTHERAPY WITH PRED, CTX, VCR, MTX, AND 6-MP PLUS RADIOTHERAPY FOR STAGE I-II NON-HODGKIN'S LYMPHOMA IN CHILDREN

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PROTOCOL NUMBER(S) SJCRH-NHL-78-I/II

OBJECTIVES:

I. Evaluate Induction therapy consisting of vincristine/prednisone/cyclophosphamide and simultaneous involved field radiotherapy followed by Maintenance therapy with 6-mercaptopurine/methotrexate in the treatment of children with non-Hodgkin's lymphoma (NHL), Stage I or II.

II. Evaluate it methotrexate as a prophylactic measure against CNS disease in patients with head/neck lymphoma.

PROTOCOL ENTRY CRITERIA: Previously untreated children (under the age of 20 years) with biopsy-proven NHL of any diffuse histologic type, Stage I or II. Patients may have received up to 1 week of steroid therapy or 1 dose of vincristine.

PROTOCOL OUTLINE: Nonrandomized study. All patients enter Induction; patients in CR following Induction proceed to Maintenance. Patients with head and neck primaries receive CNS prophylaxis concurrent with Induction and Maintenance therapy.

Induction: 2-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; plus Prednisone, PRED, NSC-10023; plus supervoltage irradiation.

Maintenance: 2-Drug Combination Chemotherapy. 6-Mercaptopurine, 6-MP, NSC-755; MTX. (Patients who develop CNS relapse receive Cytosine arabinoside, ARA-C, NSC-63878 plus MTX.)

CNS Prophylaxis. IT Methotrexate, MTX, NSC-740.

STRATIFICATION BY: Location of primary tumor (head/neck vs. other).

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, bone marrow aspiration, CSF examination, chest x-ray, skull films, skeletal survey, liver/spleen scan, bone scans, whole body gallium citrate scan, tuberculin and histoplasmin skin tests, other evaluations appropriate to particular tumor locations.

END POINTS: Response/remission rate, duration of response, survival.

CURRENT STATUS: About 30 patients will be entered over 3 years.

DOSAGE SCHEDULE:

Induction: 2000 rads to the involved field; VCR - 1.5 mg/sqm (maximum 2 mg) iv push on days 0, 7, 14, 21, 28, and 35; CTX - 600 mg/sqm iv push on days 0, 21, and 42; PRED - 40 mg/sqm/day po in 3 divided doses on days 0 through 28 and tapered. Those patients in CR at the end of a 7-10 day rest period following Induction proceed to Maintenance therapy; patients who fail to respond and those with progressive disease are transferred to another protocol.

Maintenance: 6-MP - 75 mg/sqm/day po; MTX - 30 mg/sqm/week po. Continue Maintenance for a total duration of 15 months from the time of diagnosis. Patients who develop lymphomatous relapse or leukemic conversion are removed from study. CNS relapse may be treated with it MTX (10 mg/sqm) and Cytosine arabinoside (50 mg/sqm) weekly or biweekly and external beam Radiotherapy (if it Chemotherapy fails to control relapse). Testicular relapse should be treated with Radiotherapy (1500-2000 rads).

CNS Prophylaxis: MTX - 12 mg it on days 0, 21, and 42 of Induction, then q 6 weeks during Maintenance.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

8.0040 PHASE III INDUCTION SINGLE-AGENT CHEMOTHERAPY CTX VS COMBINATION CTX/VCR/PRED WITHOUT MAINTENANCE IN NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) ARG-GATLA-1-LRS-79

OBJECTIVES:

I. Evaluate which combination is more effective in producing complete remissions and long survivals free of disease: a moderate combination chemotherapy with CTX, VCR and PRED (COP) vs. intermittent single-agent chemotherapy with CTX.

II. Compare these two schemes with more aggressive combinations COPP-CVPP-CCVPP of historic groups treated by GATLA.

PROTOCOL ENTRY CRITERIA: Patients over 20 years of age, without previous treatment, WBC count more than 4,000/cmm and platelet count more than 100,000/cmm; with histologic diagnosis of non-Hodgkin's lymphoma, nodular well differentiated, poorly differentiated, mixed and diffuse well differentiated.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. COP: Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Induction.

Arm I: CTX - 200 mg/sqm po for 5 days every 21 days for 6 months.

Arm II: CTX - 1 g/sqm iv day 1, VCR - 1.5 mg/sqm iv day 1, PRED - 60 mg/sqm po for 5 days. Repeat cycle every 21 days for 8 cycles.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: CTX - 100, 200, 1000 mg vials; VCR - 1 mg vials; PRED - 40 mg tablets.

DATE SUMMARIZED: 02/80

8.0041 CHEMOTHERAPY WITH BACOP (BLEO/ADR/CTX/VCR/PRED) VS COPP (CTX/VCR/PCB/PRED) FOR ADVANCED DIFFUSE HISTIOCYTIC LYMPHOMA

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PROTOCOL NUMBER(S) ARG-GATLA-7701; ARG-GN-1

OBJECTIVES:

I. Determine whether or not the more intensive BACOP regimen - bleomycin (BLEO)/adriamycin (ADR)/cyclophosphamide (CTX)/-vincristine (VCR)/prednisone (PRED) - is indeed superior to the COPP regimen -CTX/VCR/procarbazine (PCB)/PRED - for diffuse histiocytic lymphoma.

PROTOCOL ENTRY CRITERIA: Patients not above 70 years of age with tissue diagnosis of Stage III or IV diffuse histiocytic non-Hodgkin's lymphoma or diffuse mixed histiocytic-lymphocytic lymphoma. Patients must have adequate cardiac status.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy (C-MOPP). COPP - Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023.

Arm II: 5-Drug Combination Chemotherapy. BACOP: CTX; VCF; Adriamycin, ADR, NSC-123127; Bleomycin, BLEO, NSC-125066; PRED.

STRATIFICATION BY: Participating institutions, prior Radiotherapy.

SPECIAL STUDY PARAMETERS: Bipedal lymphangiogram, bone, liver and spleen scans, percutaneous liver biopsy, lumbar puncture.

END POINTS: Response/remission rate, objective tumor response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: COPP: CTX - 650 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm iv on days 1 and 8; PCB - 100 mg/sqm iv on days 1 through 14; PRED - 40 mg/sqm po on days 1 through 14. Repeat course after 14 to 16 days rest for 6 courses. Evaluate 1 month after final course for completeness of response.

Arm II: BACOP: CTX, VCR as in Arm I; ADR - 25 mg/sqm (maximum cumulative dose 550 mg/sqm) iv on days 1 and 8; BLEO - 5 mg/sqm iv on days 14 and 21; PRED - 60 mg/sqm po on days 14 through 28. Repeat for a total of 6 courses. Evaluate 1 month after final course.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/78

PATIENT ACCRUAL: 00111078

8.0042 BCG IMMUNOTHERAPY FOR DIFFUSE NON-HODGKIN'S LYMPHOMA BEING TREATED BY RADIOTHERAPY AND C-MOPP CHEMOTHERAPY

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PROTOCOL NUMBER(S) CAN-UICC-76002; UICC-76002; CAN-NCIC-LY1; CAN-NCIC-TO-3

OBJECTIVES:

I. Determine if BCG can increase the remission rate in selected lymphomas.

II. Determine if BCG can prolong remission in selected lymphomas.

III. Test whether this protocol improves survival in each institution (compared to historical controls).

PROTOCOL ENTRY CRITERIA: Previously untreated patients 16 to 70 years of age with a tissue diagnosis of non-Hodgkin's lymphoma, classified as diffuse lymphocytic, poorly differentiated lymphoma (DLPD) (but excluding lymphoblastic leukemia, lymphoma cutis, and patients with circulating lymphoid cells over 5000/cumm), diffuse mixed lymphocytic and histiocytic lymphoma (DM), diffuse histiocytic lymphoma (DH), or diffuse undifferentiated lymphoma (DU), and at any Stage I-IV. Patients must be free of CNS disease and have no other serious illness.

PROTOCOL OUTLINE: Randomized study, as indicated.

Induction for Stages I, IE, II or IIE disease. Regimen A: Radiotherapy, megavoltage to tumor sites. Enter complete responders (CR's) for Consolidation to Arm I.

Induction and Consolidation for Stages III, IIIE or IV disease. Randomize to Arms I or II, then enter partial responders (PR's) to Regimen B, patients with bulky disease to Regimen C, and randomize CR's to Arms III or IV for Maintenance.

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. C-MOPP: Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023.

Arm II: 3-Drug Combination Chemotherapy, Hormone Therapy, plus Immunotherapy. C-MOPP as in Arm I, plus BCG-IMH, BCG.

Regimen B: Interim Radiotherapy.

Regimen C: Consolidation Radiotherapy.

Maintenance:

Arm III: Immunotherapy. BCG.

Arm IV: No Immunotherapy.

STRATIFICATION BY: Participating institutions, disease stage.

SPECIAL STUDY PARAMETERS: Lymphangiograms, liver and bone scans, IVP/IVC, G.I. series, mediastinal tomogram, skin tests.

END POINTS: Response/remission rate, response duration, recurrence rate, objective tumor response, survival rate, survival time.

CURRENT STATUS: About 250 patients will be entered.

DOSAGE SCHEDULE:

Induction and Consolidation:

Regimen A: 3000 rads minimal tumor dose to involved site or sites, given in 3 weeks to head and neck, bone and soft-tissue lesions and those above the diaphragm or in inguinal regions. For head and neck lesions, give up to 5000 to the primary site. For intra-abdominal disease - 2500 to 3000 rads minimal tumor dose given in 4 weeks to the whole abdomen with an additional 1000 rads to the main mass if indicated. Use appropriate kidney shielding.

Arm I: C-MOPP: CTX - 650 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm iv on days 1 and 8; PCB - 100 mg/sqm po on days 1 through 14; PRED - 40 mg/sqm po on days 1 through 14. Rest for 14 days, repeat course q 28 days. Give a total of 3 courses, then evaluate.

Arm II: C-MOPP, as in Arm I; plus BCG - 40 mg containing 10 to 15 times 10 to the 6th colony-forming units/mg on days 15 and 22 of each course of C-MOPP to 4 rotated sites.

In Arm I or II, if PR except for 1 site, given Interim Radiotherapy, Regimen B. Consolidate CR with 3 more courses of Arm I or Arm II Chemotherapy; to CR with previous tumor masses greater than 6 cm, give Consolidation Radiotherapy, Regimen C. For PR with disease in multiple sites, continue Arm I or Arm II therapy until CR. Randomize all CR exiting from Arms I or II to Maintenance Arm III or IV.

Regimen B: 2000 to 3000 rads given in 2 to 3 weeks to nonresponding site. If disease recurs elsewhere, stop Radiotherapy and resume Arm I or II Chemotherapy.

Regimen C: 1500 to 2000 rads given in 3 to 4 weeks to bulky disease areas, provided neutrophil count is above 2500, platelets above 125, 000.

Maintenance:

Arm III: BCG as in Arm II, q 4 weeks.

Arm IV: No further BCG Immunotherapy.

Treat Stage I or II patients with disease progression beyond Stage II during initial Radiotherapy, Regimen A, as Stage III or IV disease and analyse separately. Remove Stage III or IV patients with disease progression after 2 courses, nonresponders after 3 courses or PR after 6 courses of Chemotherapy from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given for C-MOPP; BCG - 40 mg ampules containing 10 to 15 times 10 to the sixth colony-forming units/mg.

DATE SUMMARIZED: 11/78

PATIENT ACCRUAL: 00900978

8.0043 CHEMOTHERAPY WITH CTX, VCR, PRED, MTX, 6-MP, AND ADR WITH AND WITHOUT SURGERY FOR PEDIATRIC NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) COSTA-RICA-L278

OBJECTIVES:

I. Determine if chemotherapy with cyclophosphamide (CTX)/-vincristine (VCR)/prednisone (PRED), CTX/VCR/PRED/-methotrexate (MTX)/6-mercaptopurine (6-MP), and CTX/-adriamycin (ADR)/VCR/PRED/MTX/6-MP will lead to complete and prolonged remission and cure of non-Hodgkin's lymphoma in children.

II. Determine the influence on infiltration into the CNS of early administration, during induction, of intraspinal MTX and its continued use without prophylactic radiotherapy to the cranium.

III. Establish prospectively whether classification in abdominal stages influences prognosis.

PROTOCOL ENTRY CRITERIA: Patients under 13 years old with histologically confirmed malignant non-Hodgkin's lymphoma. Patients must have no greater than 25 percent blastic cells in the bone marrow and no prior chemo- or radiotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Enter patients with Stage IA disease to Regimen A, Stage IIA to Regimen B, Stages IG, IIG, III, and IV to Regimen C.

Regimen A: 4-Drug Combination Chemotherapy plus Hormone Therapy plus Surgery. Begin Chemotherapy after total surgical resection of tumor. Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023; 6-Mercaptopurine, 6-MP, NSC-755; Methotrexate, MTX, NSC-740.

Regimen B: 4-Drug Combination Chemotherapy plus Hormone Therapy plus Surgery. Begin Chemotherapy after total surgical resection of tumor. CTX; VCR; PRED; MTX; 6-MP.

Regimen C: 5-Drug Combination Chemotherapy plus Hormone Therapy. CTX; VCR; PRED; MTX; 6-MP; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Disease stage: IA vs. IIA vs. III, IV; histology; therapy.

SPECIAL STUDY PARAMETERS: Hepatic and renal function tests; bone and pulmonary scans; CSF examination.

END POINTS: Response/remission rate, duration of response, duration of survival, relapse rate, relapse site.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Total Surgical Resection of tumor. CTX - 600 mg/sqm iv on days 1, 15, 30 and 45; VCR - 1.5 mg/sqm iv on days 1, 8, 15, 22, 30, 38 and 45; PRED - 40 mg/sqm po on days 1 through 45. Then begin Maintenance as follows: 6-MP - 75 mg/sqm po daily; MTX - 30 mg/sqm po q 8 days. Continue for 40 weeks or until relapse.

Regimen B: Total Surgical Resection of tumor. CTX, VCR, PRED as in Regimen A; MTX - 12 mg/sqm administered to the cerebrospinal fluid (intra-CSF) on days 8, 22, 38. Then begin Maintenance as follows: 6-MP, MTX as in Regimen A plus MTX - 12 mg/sqm intra-CSF monthly for 10 doses or until relapse.

Regimen C: CTX, VCR, PRED as in Regimen A; MTX - 12 mg/sqm intra-CSF on days 8, 22, 38; ADR - 40 mg/sqm iv on days 1, 15, 30, 45. Then begin Maintenance: 6-MP - 75 mg/sqm po daily; MTX - 30 mg/sqm po q 8 days. Continue for 80 weeks. CTX - 60 mg/sqm iv monthly; ADR - 40 mg/sqm iv monthly. Continue for 6 courses. MTX - 12 mg/sqm intra-CSF monthly for 10 doses or until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

8.0044 PHASE II TOTAL BODY IRRADIATION FOR STAGE III AND IV NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) POL-NHL-1

OBJECTIVES:

I. Determine the efficacy of total body irradiation for advanced centrocytic and centroblastic lymphoma.

II. Determine tolerance and toxicity of total body irradiation.

PROTOCOL ENTRY CRITERIA: Patients over 14 years of age with Stage III and IV centrocytic and centroblastic lymphoma (Lennert classification) who have received either prior therapy or no prior therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Co-60 source.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Length of survival, objective response, toxicity/morbidity of treatment.

CURRENT STATUS: 10 patients are being treated as of March 1980; a total of 30 patients will be entered.

DOSAGE SCHEDULE:

Co-60 - 200 rads midrectal dose in 20 fractions 3 times per week. Additional booster fields may be given for residual disease for a total given dose of 1000-2000 rads if tolerance is not exceeded.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

Summary as provided by investigator.

DATE SUMMARIZED: 10/80

8.0045 RADIOTHERAPY WITH OR WITHOUT CHEMOTHERAPY WITH ADR/VP-16, CMM/VP-16, OR CMM FOR LYMPHOCYTIC LYMPHOMA

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PROTOCOL NUMBER(S) SAFR-CT-LEU/LYM-A

OBJECTIVES:

I. Compare radiotherapy plus chemotherapy with adriamycin/VP-16213 or carminomycin/VP-16213 or carminomycin with radiotherapy alone in patients with lymphocytic lymphoma.

II. Evaluate the cardiotoxicity of the treatment.

PROTOCOL ENTRY CRITERIA: Patients with pathological Stage I and II lymphocytic lymphoma of the following types: large cell, including mixed large and small cell histology; small cell (atypical, intermediate lymphocytic and lymphoblastic); follicular histology and small cell diffuse (well differentiated). Patients with Stage III and IV diffuse lymphoma (small cell, atypical) are eligible.

PROTOCOL OUTLINE: All patients are treated on Regimen A. Patients with large cell lymphoma proceed to Regimen B. Patients with small cell atypical disease are randomized to Arms I and II. Patients with follicular and small cell well-differentiated disease are treated on Regimen A only.

Regimen A: Radiotherapy. Supra-diaphragmatic and abdominal irradiation.

Regimen B: 2-Drug Combination Chemotherapy. VP-16213, VP-16, NSC-141540; Adriamycin, ADR, NSC-123127.

Arm I: Single-agent Chemotherapy. Carminomycin, CMM, NSC-180024.

Arm II: 2-Drug Combination Chemotherapy. CMM; VP-16.

STRATIFICATION BY: Histologic type: large cell vs. small cell vs. follicular and small cell diffuse.

SPECIAL STUDY PARAMETERS: Cytochemical studies of blood and bone marrow, immunologic classification, functional characteristics of lymphocytes, cardiologic assessment.

END POINTS: Response/remission rate, the relationship of response to survival, quality of life, immune competence, cardiotoxicity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Radiotherapy - 3500 rads in 4.5 weeks for supradiaphragmatic disease; plus 3000 rads in 4.5 weeks for abdominal disease.

Regimen B: Induction: VP-16 - 60 mg/sqm iv infusion over 30 minutes daily for 5 days; ADR - 40 mg/sqm iv infusion over 30 minutes on day 5. Drug administration is followed by a 16-day rest period; three courses of treatment are given. Maintenance: VP-16 - 60 mg/sqm po weekly for 3 weeks. Reinduction: Repeat Induction; then start second Maintenance cycle. Continue treatment for 6 months.

Arm I: CMM - 20 mg/sqm iv infusion q 3 weeks.

Arm II: VP-16 - 60 mg/sqm iv daily for 5 days; CMM - 20 mg/sqm iv infusion over 30 minutes on day 5. Repeat q 3 weeks.

Patients who relapse after less than one year of treatment proceed to protocol SAFR-CT-LEU/LYM-B.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

8.0046 CHEMOTHERAPY WITH VP-16/ADR VS CHOP (CTX/ADR/VCR/PRED) VS VP-16/CMM FOR LARGE CELL LYMPHOCYTIC LYMPHOMA

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PROTOCOL NUMBER(S) SAFR-CT-LEU/LYM-C

OBJECTIVES:

I. Compare previous results obtained with the combination VP-16213/adriamycin with results obtained in this study using CHOP (cyclophosphamide/adriamycin/vincristine/prednisone).

II. Determine whether 4-drug regimens such as CHOP are superior to 2-drug regimens (adriamycin/VP-16213 or carminomycin/VP-16213).

PROTOCOL ENTRY CRITERIA: Patients with pathological Stage III and IV lymphocytic lymphoma (large cell, including mixed large and small cell histology). Disease histology must be confirmed by cytochemistry and ultrastructure.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. VP-16213, VP-16, NSC-141540; Adriamycin, ADR, NSC-123127.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; ADR; plus Prednisone, PRED, NSC-10023.

Arm III: 2-Drug Combination Chemotherapy. VP-16; Carminomycin, CMM, NSC-180024.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Cytochemical studies of blood and bone marrow, immunologic classification, functional characteristics of lymphocytes.

END POINTS: Response/remission rate, the relationship of response to survival, quality of life, immune competence.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Induction: VP-16 - 60 mg/sqm iv infusion over 30 minutes daily for 5 days; ADR - 40 mg/sqm iv infusion over 30 minutes on day 5. Drug administration is followed by a 16-day rest period; 3 courses of treatment are given. Maintenance: VP-16 - 60 mg/sqm po weekly for 3 weeks. Reinduction: Repeat Induction; then start second Maintenance cycle.

Arm II: CHOP: CTX - 750 mg/sqm iv infusion over 30 minutes on day 1; ADR - 40 mg/sqm iv infusion over 30 minutes on day 1; VCR - 1.4 mg/sqm iv on days 1 and 8; PRED - 45 mg/sqm po daily on days 1 through 10. Repeat course after an 11-day rest period.

Arm III: Induction: VP-16 - 60 mg/sqm as in Arm I; CMM - 20 mg/sqm iv infusion over 30 minutes on day 5. Drug administration is followed by a 16-day rest period; 3 courses of treatment are given. Maintenance: VP-16 as in Arm I. Reinduction: VP-16; CMM as in Induction; then start second Maintenance cycle.

Patients are evaluated q 6 months. Failures on Arm I cross over to Arm II; failures on Arm II are rerandomized to Arms I and III, and failures on Arm III switch to Arm II.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

8C. LYMPHOMA—GENERAL

8.0047 PHASE II CHEMOTHERAPY WITH AMSA FOR REFRACTORY HODGKIN'S AND DIFFUSE HISTIOCYTIC OR LYMPHOCYTIC LYMPHOMA

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PROTOCOL NUMBER(S) CLB-7972

OBJECTIVES:

I. Determine the complete or partial response frequency of refractory Hodgkin's disease, diffuse histiocytic and poorly differentiated lymphocytic lymphoma to treatment with m-AMSA.

II. Determine the duration of response to continued administration of m-AMSA.

III. Provide clinical and laboratory data regarding toxicity.

PROTOCOL ENTRY CRITERIA: Patients with measurable and histologically diagnosed Stage III or IV Hodgkin's disease, diffuse histiocytic or poorly differentiated lymphocytic lymphoma refractory to standard combination chemotherapy. Patients must have a survival potential of 2 months or more and have adequate hematologic and liver function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Kidney function tests: BUN, creatinine; liver function tests: SGOT/SGPT; lymphangiogram; liver/spleen scan.

END POINTS: Response/remission rate, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 75 to 90 patients will be entered in 10 to 12 months.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm in 5% dextrose solution iv infusion on day 1 q 3 weeks (60 mg/sqm for patients previously heavily treated with chemotherapy or patients with hepatic dysfunction). Increase dose for each course by 20 mg/sqm over previous dose until maximum dose is 160 mg/sqm or until myelosuppression occurs. Give palliative CNS radiation as needed. Continue treatment until relapse or progression. Remove patients with progression from study after 2 courses at maximum dose.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 20 and 50 mg vials.

DATE SUMMARIZED: 11/79

8.0048 PHASE II SINGLE-AGENT CHEMOTHERAPY WITH N-(PHOSPHONOACETYL)-L-ASPARTATE OR AMSA FOR PREVIOUSLY TREATED LYMPHOMA

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PROTOCOL NUMBER(S) EST-1480

OBJECTIVES:

I. Determine objective response rate, duration of remission, and toxicity of N-(phosphonoacetyl)-L-aspartate (PALA) and m-AMSA in patients with Stages III or IV (Ann Arbor classification) Hodgkin's disease and nodular or diffuse non-Hodgkin's lymphomas who have failed on other chemotherapeutic regimens.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven Stage III or IV Hodgkin's disease and non-Hodgkin's lymphomas of diffuse or nodular type not amenable to curative treatment. Patients may have locally recurrent disease not amenable to further radiation therapy but may not be in the leukemic phase of their disease. Patients must have had at least one but not more than two prior chemotherapy trials and have failed or relapsed. Patients may not have previously been treated with the protocol agents, and they must have at least one objective measurable disease parameter. Cytotoxic therapy must have ceased at least 3 weeks (6 weeks for nitrosoureas) prior to entry. Bone marrow, liver, and kidney function must be adequate although patients with WBC less than 4000 and platelets less than 100,000 are eligible for the PALA arm of the study. Patients must be between 15 and 76 years of age, free from serious infection, and have an ECOG performance status of 0-2.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. N-(phosphonoacetyl)-L-aspartate, PALA, NSC-224131.

Arm II: Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions, histology (Hodgkin's vs. nodular non-Hodgkin's vs. diffuse non-Hodgkin's), performance status (0-1 vs. 2), weight loss (less than 5 percent vs. 5 percent or more).

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic parameters, kidney and liver function tests.

END POINTS: Response/remission rate, duration of response, objective tumor response, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 40-50 patients will be entered onto each arm.

DOSAGE SCHEDULE:

Arm I: PALA - 2.5 g/sqm/day iv infusion for 2 days; repeat course every 2 weeks for a minimum of 2 cycles. CR continue for 10 more courses, PR and those with stable disease continue to progression or relapse, and patients with progressive disease go off study.

Arm II: AMSA - 30 mg/sqm/day for 3 days iv infusion. Repeat q 3 weeks for a minimum of 2 courses. CR continue for 6 more cycles of treatment. PR and those with stable disease continue to progression or relapse, and patients with progressive disease go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 1 g ampules; AMSA - 75 mg ampules.

DATE SUMMARIZED: 07/80

8.0049 PHASE II STUDY OF GALLIUM NITRATE FOR HODGKIN'S AND NON-HODGKIN'S LYMPHOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7912

OBJECTIVES:

I. Determine the efficacy, as measured by response rate, of gallium nitrate in patients with malignant lymphoma, both Hodgkin's and non-Hodgkin's types, in patients who have received prior therapy and are not eligible for higher priority studies.

II. Determine the nature and degree of toxicity of this drug.

PROTOCOL ENTRY CRITERIA: Patients with clearly measurable disease of malignant lymphoma, with a life expectancy of at least 6 weeks and a performance status of at least 2 (Karnofsky 50 to 60). Patients must have adequate hematologic, renal, liver and cardiac status and those with prior cis-platinum therapy must have a creatinine clearance of at least 70 cc/min. 4 weeks must have elapsed since prior therapy, hematologic recovery must be evident and no concomitant therapy is permitted.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Gallium nitrate, NSC-15200.

STRATIFICATION: Prior cis-platinum therapy: yes vs. no.

SPECIAL STUDY PARAMETERS: Gallium scan, audiogram, IVP or renal scan, 24-hour urine protein.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival time.

CURRENT STATUS: 50 to 75 patients will be entered in one year.

DOSAGE SCHEDULE:

Gallium nitrate - 700 mg/sqm iv infusion given over 30 minutes in 200 ml NS q 2 weeks. Give all patients 2 liters of fluid over their normal intake po or iv within 12 hours prior to Gallium nitrate administration. Additionally, just before Gallium nitrate give a 500 cc normal saline infusion over 2 hours. Do not repeat course until bone marrow has recovered (wbc at least 3000, platelets at least 100,000). Give a minimum of 2 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Gallium nitrate - 10 ml ampules.

DATE SUMMARIZED: 10/79

PATIENT ACCRUAL: 00180779

8.0050 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED HODGKIN'S AND NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) SWOG-7918

OBJECTIVES:

I. Determine the antitumor activity and toxicity of AMSA used as a single dose in patients with Hodgkin's and non-Hodgkin's lymphoma who have failed on higher priority protocols.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven advanced Hodgkin's or non-Hodgkin's lymphocytic or histiocytic lymphoma who are not eligible for any higher priority protocols. Patients must have a minimum life expectancy of 6 weeks and a Karnofsky performance status of 50 or better. Patients must have adequate renal and hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate; duration of response; toxicity/morbidity of treatment; objective tumor response.

CURRENT STATUS: 75 patients will be entered in 1 year.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv infusion on day 1. Begin therapy of poor-risk patients (those over 65 years old or with prior whole abdominal or pelvic radiation or severe myelosuppression) at 90 mg/sqm, of patients with abnormal liver function at 90 mg/sqm (if bilirubin is less than 3 but greater than 1.2), or 60 mg/sqm (if bilirubin is 3 or over or alkaline phosphatase and SGOT are 3 times normal or greater). Repeat course q 3 to 4 weeks as toxicity permits. Remove patients after 2 courses for sustained hepatic toxicity, other toxicity, or progressive or unsatisfactory stable disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 20 and 75 mg vials.

DATE SUMMARIZED: 11/79

8.0051 PHASE II PILOT CHEMOTHERAPY WITH DAVA/BCNU/ADR/PRED FOR REFRACTORY HODGKIN'S AND NON-HODGKIN'S LYMPHOMA

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PROTOCOL NUMBER(S) SWOG-7967

OBJECTIVES:

I. Evaluate the frequency and completeness of response to chemotherapy with EBAP: vindesine (DAVA)/BCNU/adriamycin (ADR)/prednisone (PRED) in patients with malignant lymphoma (non-Hodgkin's disease and Hodgkin's disease) who have received prior therapy and are not eligible for higher priority studies; and compare these results to previous SWOG experience with VBAP.

PROTOCOL ENTRY CRITERIA: Patients with measurable Hodgkin's or non-Hodgkin's lymphoma refractory to prior therapy who are ineligible for higher priority protocols. Patients must have adequate cardiac status and must not have had prior nitrosourea therapy or more than 390 mg/sqm of prior ADR.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy plus Hormone Therapy. Vindesine, DAVA, NSC-245467; BCNU, NSC-33299; Adriamycin, ADR, NSC-123127; Prednisone, PRED, NSC-10023.

STRATIFICATION: Participating institutions, disease type.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, objective tumor response, relapse rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 50 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 2 mg/sqm iv on day 1; BCNU - 30 mg/sqm iv on day 1; ADR - 30 mg/sqm (maximum cumulative dose 550 mg/sqm; maximum dose 60 mg) iv on day 1; PRED - 60 mg/sqm po on days 1 through 4. Decrease dosage of DAVA, BCNU and ADR by 25% for poor-risk patients (over 70 years of age, with persistent granulocyte count between 1500 and 2500, and bilirubin greater than 1.3 mg %); decrease BCNU only when creatinine is greater than 2.5%.

Repeat course q 21 days as hematologic toxicity permits. Continue therapy until disease progression eliminating ADR when maximum cumulative dose is reached. Give a maximum of 2 courses for an adequate trial.

Dosage modifications for toxicity and for patients with prior mediastinal radiotherapy are given.

DOSAGE FORMS: ADR - 10 mg and 50 mg vials; BCNU - 100 mg vials; PRED - 5 and 50 mg tablets; DAVA - 5 mg ampules.

DATE SUMMARIZED: 12/79

8.0052 PHASE II PILOT CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE FOR REFRACTORY MALIGNANT LYMPHOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-8005

OBJECTIVES:

I. Determine response rate and response duration in patients with refractory malignant lymphoma, both Hodgkin's disease and non-Hodgkin's lymphoma treated with dihydroxyanthracenedione used in a single dose every-three-week schedule.

II. Define the qualitative and quantitative toxicities of dihydroxyanthracenedione administered in a Phase II study.

PROTOCOL ENTRY CRITERIA: Patients of all ages with malignant lymphoma with clearly measurable disease who are ineligible for higher priority Southwest Oncology Group protocols. Patients must have a life expectancy of at least 6 weeks and a performance status of 2 or better (Karnofsky 50-60). No other chemotherapeutic agents or radiotherapy may be given concomitantly. Patients must be fully recovered from prior therapy and have a pretreatment WBC of 3500/cumm or greater, and a platelet count of 125,000/cumm or greater. Four weeks must have elapsed for patients receiving prior chemotherapy or radiotherapy and the nadirs of leukopenia and thrombocytopenia must have been surpassed with evidence of hematologic recovery.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: CAT; x-ray; bone marrow biopsy; hematologic, renal and hepatic function tests.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 14-25 patients will be entered for each disease category.

DOSAGE SCHEDULE:

DHAD - 12 mg/sqm iv infusion through a free-running iv over 30 minutes q 3 weeks, provided patient has recovered from previous drug-induced toxicity. Patients with progressive disease after 2 courses and those who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 5 mg ampules.

DATE SUMMARIZED: 10/80

8.0053 PHASE II CHEMOTHERAPY WITH SPIROGERMANIUM FOR REFRACTORY LYMPHOMA

Kaplan, R. S., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America

PROTOCOL NUMBER(S) BCRP-8005

OBJECTIVES:

I. Determine the frequency and duration of response to spirogermanium in patients with lymphoma refractory to standard therapy; the duration of response will be determined while the patient is maintained on continuous therapy.

II. Analyze the relationship of quality of response to survival of the patient.

III. Determine the acute, chronic and cumulative toxicity of the dose regimen.

IV. Analyze the ability of the preclinical system to prospectively predict the antitumor activity and both quantitative and qualitative toxicology of spirogermanium.

PROTOCOL ENTRY CRITERIA. Patients under 70 years of age with histologically documented malignant lymphoma of Hodgkin's or non-Hodgkin's type, who have failed primarily or secondarily all appropriate standard forms of chemotherapy, e.g., MOPP plus SCAB, CAVP or CVP, etc. Patients with prior radiotherapy must have measurable disease either outside radiotherapy ports or within ports if there is documented progression after irradiation in those specific areas. Patients must have no history of seizure or CNS metastases. Liver and kidney function tests must be normal, and patients must be ambulatory.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Spirogermanium, NSC-192965.

STRATIFICATION BY: None given

SPECIAL STUDY PARAMETERS: BUN, creatinine, serum calcium and phosphorus, SGOT, alkaline phosphatase, bilirubin, chest x-ray, appropriate scans, tumor measurements.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 20-30 patients in each disease category will be entered.

DOSAGE SCHEDULE:

Spirogermanium - 50 mg/sqm iv 30-minute infusion on days 1, 3, 5, 8, 10 and 12, then one day q week. Continue treatment until progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Spirogermanium - 100 mg vials.

DATE SUMMARIZED: 10/80

8.0054 SEQUENTIAL CHEMOTHERAPY WITH IMVP-16 (IPP/MTX/VP-16), HOP (ADR/VCR/PRED), OR OAP-BLEO (ARA-C/BLEO/PRED/VCR) FOR STAGE IV LARGE CELL LYMPHOMA

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PROTOCOL NUMBER(S) MDAR-406; MDA-DT-8032

OBJECTIVES:

I. Assess the efficacy of the combination IMVP-16 (ifosfamide/methotrexate/VP-16213) in increasing the complete remission rate in patients with Stage IV large cell lymphoma.

II. Assess the efficacy of late Intensification therapy with HOP (adriamycin/vincristine/prednisone) or with OAP-BLEO (cytosine arabinoside/bleomycin/prednisone/vincristine) in prolonging the duration of CR.

III. Assess the efficacy of CNS prophylaxis with systemic cytosine arabinoside and high-dose methotrexate.

PROTOCOL ENTRY CRITERIA: Patients with Stage IV large cell lymphoma (including nodular or diffuse histiocytic, nodular or diffuse mixed, and immunoblastic sarcoma) with evaluable lesions. Patients must have recovered from the toxic effects of any prior radiotherapy unless the clinical situation is so urgent that initiation of chemotherapy is necessary before recovery.

PROTOCOL OUTLINE: Nonrandomized study. All patients enter Regimen A. Patients not in CR after 3 courses and those showing progression after 1 course or minimal response after 2 courses cross over to Regimen B (patients with radiographic evidence of cardiac failure cross over to Regimen C instead of Regimen B). Patients in CR after 3 courses of Regimen A proceed to late Intensification with Regimen C. Patients at high risk of CNS relapse receive CNS prophylaxis treatment starting with the third course of Regimen A.

Regimen A: 3-Drug Combination Chemotherapy. IMVP-16: Ifosfamide, IPP, NSC-109724; Methotrexate, MTX, NSC-740; VP-16213, VP-16, NSC-141540.

Regimen B: 2-Drug Combination Chemotherapy plus Hormone Therapy. HOP: Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Prednisone, PRED, NSC-10023.

Regimen C: 3-Drug Combination Chemotherapy plus Hormone Therapy. OAP-BLEO: Cytosine arabinoside, ARA-C, NSC-63878; Bleomycin, BLEO, NSC-125066; PRED; VCR.

CNS Prophylaxis: Single-agent Chemotherapy. MTX, high-dose and intrathecal.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Granulocyte and platelet counts.

END POINTS: Response/remission rate, objective tumor response, duration of remission.

CURRENT STATUS: An estimated 25 to 30 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: IMVP-16: (Patients under 65 with no prior Radiotherapy) IPP - 1 g/sqm iv daily for 5 days; MTX - 30 mg/sqm im on days 3 and 10; VP-16 - 120 mg/sqm iv daily for 3 days; (Patients over 65 with extensive prior Radiotherapy) IPP - 1 g/sqm iv daily for 5 days; MTX - 25 mg/sqm im on days 3 and 10; VP-16 - 90 mg/sqm iv daily for 3 days. Course is repeeated q 21 days, depending upon myelosuppression.

Regimen B: HOP: (Patients with adequate marrow reserve) ADR - 80 mg/sqm iv; VCR - 1.4 mg/sqm iv; PRED - 100 mg po daily for 5 days; (Patients with poor marrow reserve receive ADR reduced dose - 60 mg/sqm iv). Course is repeated q 21 days, depending upon myelosuppression.

Regimen C: Intensification: OAP-BLEO: ARA-C - 75 mg/sqm in 4 fractions sc daily for 5 days; BLEO - 15 U im on days 1 and 5; PRED - 100 mg po daily for 5 days; VCR - 1.4 mg/sqm iv on day 1. Course is repeated q 21-28 days, depending upon myelosuppression.

CNS Prophylaxis: Patients at high risk of CNS relapse do not receive the day 10 MTX dose on Regimen A during the first 3 courses. Starting with the 4th course, prophylactic high-dose MTX and intrathecal MTX are given for 3 courses.

Patients who do not achieve CR on IMVP-16 but do achieve CR on HOP stay on HOP until 480 mg/sqm cumulative dose of ADR is reached, then proceed to late Intensification with OAP-BLEO. Patients who fail to achieve CR on IMVP-16 or HOP change to OAP-BLEO treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

8.0055 PHASE II COMBINATION CHEMOTHERAPY WITH METHYL-GAG/VM-26 FOR ADVANCED MALIGNANT LYMPHOMA

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PROTOCOL NUMBER(S) MSKCC-8081

OBJECTIVES:

I. Evaluate the antitumor activity and toxicity of methyl-GAG and VM-26 in combination for the treatment of patients with advanced malignant lymphoma.

II. Evaluate the appropriate dosage, toxicities and pharmacokinetics of these agents.

PROTOCOL ENTRY CRITERIA: Patients with Hodgkin's disease, non-Hodgkin's lymphoma and mycosis fungoides who have failed conventional chemotherapy protocols and are ineligible for protocols of higher priority. There must be histologic confirmation of active disease and bidimensionally measurable disease parameters. Patients must have a Karnofsky performance status of at least 50 and there must be adequate hematologic, renal and hepatic function; they must not have received chemotherapy or radiotherapy within 3 weeks prior to entry (6 weeks for nitrosoureas).

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Methyl-GAG, MeGAG, NSC-32946; VM-26, NSC-122819.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: CBC, platelet count differential smear, hepatic and renal function tests, radiologic studies to evaluate tumor response.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: The entry of approximately 35 patients into this trial is anticipated.

DOSAGE SCHEDULE:

MeGAG - 600 mg/sqm/week; VM-26 - 100 mg/sqm/week for good-risk patients (those with a performance status greater than 70, no evident myelophthisis, no extensive prior radiation to bone marrow containing areas). Poor-risk patients receive reduced doses: MeGAG - 500 mg/sqm; VM-26 - 75 mg/sqm/week. A minimum of 2 courses is required for an adequate trial. Chemotherapy is discontinued whenever unacceptable side effects or life-threatening effects develop.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

8.0056 CHEMOTHERAPY FOR STAGE III/IV DIFFUSE LYMPHOMAS WITH PROMACE (CTX/ADR/VP-16/PRED/MTX) AND MOPP (NM/VCR/PCB/PRED)

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PROTOCOL NUMBER(S) NCI-78-C-34; NCI-MB-93

OBJECTIVES:

I. Increase CR rate and long-term survival of patients with advanced diffuse lymphomas using ProMACE (cyclophosphamide/adriamycin/VP-16213/prednisone/methotrexate) for Induction and late Intensification and MOPP (nitrogen mustard/vincristine/procarbazine/prednisone) for Consolidation.

II. Prevent tumor regrowth during periods of marrow hypoplasia with high-dose methotrexate therapy.

III. Test the kinetic hypothesis that late Intensification will increase the number of patients achieving long-term disease-free survival.

IV. Determine the effect of hyperalimentation in a random study of this therapeutic modality.

V. Determine the prognostic significance of lymphocyte surface markers.

VI. Determine the distribution of corticosteroid hormone receptors in adult diffuse non-Hodgkin's lymphomas.

VII. Prevent CNS relapse in bone marrow-positive cases using cranial irradiation and high-dose methotrexate.

VIII. Prevent gastrointestinal perforation by surgical removal of intestinal tumor prior to chemotherapy.

IX. Use the rate of response as the determinant of duration of treatment.

PROTOCOL ENTRY CRITERIA: Patients with a tissue diagnosis of diffuse poorly differentiated lymphocytic lymphoma, diffuse mixed histiocytic-lymphocytic lymphoma, diffuse histiocytic lymphoma, or diffuse undifferentiated lymphoma of Stages III-IV and Stage II with abdominal disease. Previously untreated patients are preferred, but consideration will be given to those with limited prior radiotherapy. Patients should be under the age of 65 years.

PROTOCOL OUTLINE: Partially randomized study. Enter patients with potentially resectable gastrointestinal disease to Regimen A and others to Regimen B. Randomize patients in Regimen B to receive total parenteral hyperalimentation or standard nutrition.

Regimen A: Surgery.

Regimen B:

Induction: 4-Drug Combination Chemotherapy plus Hormone Therapy. ProMACE: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; VP-16213, VP-16, NSC-141540; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590; Prednisone, PRED, NSC-10023.

Consolidation: 2-Drug Combination Chemotherapy plus Hormone Therapy with or without Radiotherapy. MOPP: Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; PRED.

Late Intensification: 3-Drug Combination Chemotherapy plus Hormone Therapy. ProMACE.

STRATIFICATION BY: Gastrointestinal involvement (yes vs. no), bone marrow involvement (yes vs. no), histology (DPDL vs. DHL, DML, DUL), disease stage (III vs. IV-marrow, IV-GI, and II-abdominal vs. IV-other).

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, chest x-ray, KUB, EKG, GI series, other x-rays and scans as indicated clinically.

END POINTS: Response/remission rate, duration of response, disease-free interval, survival, toxicity/morbidity of treatment.

CURRENT STATUS: About 33 patients will be entered in 4 years.

DOSAGE SCHEDULE:

Regimen A: Surgical debulking for those patients in whom 95 percent of abdominal disease can be resected. Patients proceed to Regimen B 10 days to 2 weeks postoperatively.

Regimen B:

Induction. ProMACE: CTX - 650 mg/sqm iv on days 1 and 8; ADR - 25 mg/sqm iv on days 1 and 8 (total cumulative dose not to exceed 550 mg/sqm); VP-16 - 120 mg/sqm iv over 30 minutes on days 1 and 8; PRED - 60 mg/sqm/day po on days 1 through 14; MTX - 1.5 g/sqm iv infusion over 12 hours beginning on day 14 with adequate hydration before, during, and after treatment; CF - 50 mg/sqm iv 24 hours after the beginning of the MTX infusion, then 50 mg/sqm po q 6 hours for a total of 4 oral doses. Repeat q 28 days. Continue treatment until the rate of response decreases or until 1 cycle after CR.

Consolidation. MOPP: NM - 6 mg/sqm iv on days 1 and 8; VCR - 1.4 mg/sqm iv on days 1 and 8; PCB - 100 mg/sqm/day po on days 1 through 14; PRED - 60 mg/sqm/day po on days 1 through 14. Patients with bone marrow involvement receive 2400 rads of prophylactic cranial irradiation with first cycle of Consolidation therapy. Repeat Consolidation cycles q 28 days. Patients in CR at beginning of Consolidation receive the same number of Consolidation cycles as Induction cycles. Patients with responding residual disease continue Consolidation until 1 cycle beyond CR or until the rate of tumor response decreases. Patients with progressive disease at the beginning of Consolidation receive MOPP for 2 cycles after CR or until progressive disease recurs. Patients with progressive disease during Induction receive no Chemotherapy beyond Consolidation.

Late Intensification. ProMACE: Give the same number of cycles as was given during Induction. Repeat cycles at 56-day intervals.

A patient goes off study when there is a 50 percent increase of measurable tumor during either late Intensification or Consolidation if he has already progressed during Induction.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

8.0057 TBI PLUS CHEMOTHERAPY WITH ARA-C/CTX PLUS AUTOLOGOUS BONE MARROW THERAPY FOR RECURRENT LYMPHOMA

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PROTOCOL NUMBER(S) NCI-79-C-93; NCI-POB-7806

OBJECTIVES:

I. Investigate the utility of a combination of aggressive chemotherapy with cytosine arabinoside/cyclophosphamide and total body irradiation (TBI) with autologous bone marrow infusion in the treatment of recurrent disseminated non-Hodgkin's lymphoma.

II. Study the utility of flow-micro-fluorimetric techniques as a potential means of individualizing timed-sequence chemotherapy scheduling.

III. Study the value of supplementary irradiation to apparently localized recurrent tumor.

IV. Study recurrent tumor for changes in morphology, surface receptors, EBV virus genome, and cell surface micro-viscosity as compared to the patient's primary tumor.

PROTOCOL ENTRY CRITERIA: All patients with recurrent non-Hodgkin's lymphoma treated with NCI Protocol 77-04 (NCI-77-C-145) from whom autologous marrow has been stored for at least 2 months prior to relapse. Patients may have relapsed locally and been treated with local therapy, and then relapsed again. Patients who otherwise qualify but in whom some complicating factor exists (e.g., renal failure, bone marrow hypoplasia, cardiac dysfunction, etc.) will be considered individually. Patients with prior CNS disease proven resistant to chemotherapy and cranial or craniospinal radiation will normally be ineligible, but will be considered individually.

PROTOCOL OUTLINE: Study randomized for hyperalimentation only.

2-Drug Combination Chemotherapy plus Radiotherapy plus Immunotherapy. Cytosine arabinoside, ARA-C, NSC-63878; Cyclophosphamide, CTX, NSC-26271; plus TBI; plus autologous marrow infusion.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hemogram, electrolytes, liver and kidney function studies, chest x-ray, EKG, full chemistry profile and coagulation studies, echocardiogram, marrow aspiration and biopsy, CSF examination, gallium scan, abdominal CAT scan, ultrasound.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

CTX - 45 mg/kg iv over 30 minutes on days 1, 2, 3, and 4; ARA-C - 300 mg/sqm/day iv by continuous 24-hour infusion on days 9 through 12; plus total body irradiation - either 15 rads/day for 8 fractions omitting weekends beginning on day 1 or 400 rads on days 6 and 8. Autologous marrow infusion is administered on day 13. Local irradiation of 2000 rads given in one week may be considered in a few patients with bulk disease prior to or during therapy. Patients will be partially restaged q month for the first 6 months, then q 3 months for 6 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

SECTION 9

MELANOMA AND OTHER SKIN CANCERS

NCOG-10M81 PHASE II ENDOCRINE THERAPY WITH TAMOXIFEN FOR STAGE III MELANOMA RESISTANT TO DTIC THERAPY 9.0001
NCOG-7O81 PHASE I-II HEAVY CHARGED PARTICLE RADIOTHERAPY OF LOCALIZED OCULAR CHOROIDAL MELANOMA 9.0002
RTOG-8004 PHASE I/II RADIOTHERAPY WITH FAST NEUTRONS FOR METASTATIC MALIGNANT MELANOMA 9.0003
SEG-MEL-P42 PILOT STUDY OF CHEMOTHERAPY WITH DIBROMODULCITOL (DBD) FOR INCURABLE MALIGNANT MELANOMA 9.0004
SEG-77MEL0203 PHASE III RANDOMIZED CONTROLLED ADJUVANT STUDY OF C. PARVUM IMMUNOTHERAPY FOR STAGE I MELANOMA 9.0005
SEG-77MEL0303 PHASE III SURGICAL ADJUVANT IMMUNOTHERAPY WITH CORYNEBACTERIUM PARVUM VS BCG FOR LIMITED STAGE II MELANOMA 9.0006
SEG-77MEL0403 PHASE III COMPARISON OF DTIC/CTX/C. PARVUM VS C. PARVUM ALONE AS ADJUVANT THERAPY FOR STAGE II-III MELANOMA 9.0007
SWOG-7521 PHASE III CHEMOTHERAPY WITH BHD (BCNU/DTIC/HU) WITH OR WITHOUT BCG IMMUNOTHERAPY FOR HIGH-RISK MELANOMA PATIENTS 9.0008
SWOG-7727/28 PHASE III CHEMOTHERAPY WITH BHD (BCNU/HU/DTIC) AND LEVAMISOLE IMMUNOTHERAPY VS DTIC/ACT-D FOR DISSEMINATED MELANOMA 9.0009
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SECTION 9

MELANOMA AND OTHER SKIN CANCERS

9.0001 PHASE II ENDOCRINE THERAPY WITH TAMOXIFEN FOR STAGE III MELANOMA RESISTANT TO DTIC THERAPY

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PROTOCOL NUMBER(S) NCOG-10M81

OBJECTIVES:

I. Determine the activity of the antiestrogen tamoxifen (TMX) in the treatment of disseminated malignant melanoma in patients who have failed conventional chemotherapy.

II. Design a Phase III study exploring TMX as part of the initial treatment of disseminated malignant melanoma if this treatment has been shown to be active in participants of this study.

PROTOCOL ENTRY CRITERIA: Patients with measurable, biopsy proven, NCOG Stage III melanoma who have failed prior therapy which included DTIC. Patients must have a minimum life expectancy of 8 weeks, a Karnofsky performance status of 50% or better, and adequate hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Single-agent Antiestrogen Therapy. Tamoxifen, TMX, NSC-180973. Low dose.

Regimen B: Single-agent Antiestrogen Therapy. TMX. High dose.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Bone, liver, and brain scans, estrogen receptor status.

END POINTS: Objective tumor response, survival time, response/remission rate.

CURRENT STATUS: 25 patients will be entered in about 10 months.

DOSAGE SCHEDULE: Enter all patients to Regimen A initially.

Regimen A: TMX - 40 mg/day po for 3 weeks. Evaluate patients, enter patients with disease progression to Regimen B, continue therapy for all others for 3 additional weeks before re-evaluation. If disease progresses at this point remove patient from study. Continue TMX therapy for other patients until disease progression.

Regimen B: TMX - 80 mg/day po for 3 weeks. Evaluate patients, if disease progression has occurred remove patient from study. Continue therapy for all others until disease progression.

Concomitant Radiotherapy for CNS metastases or medication to reduce cerebral edema are permitted.

Dosage modifications for toxicity are given.

DOSAGE FORMS: TMX - 10 mg tablets.

DATE SUMMARIZED: 12/79

9.0002 PHASE I-II HEAVY CHARGED PARTICLE RADIOTHERAPY OF LOCALIZED OCULAR CHOROIDAL MELANOMA

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PROTOCOL NUMBER(S) NCOG-7O81; RTOG-7908

OBJECTIVES:

I. Evaluate the effectiveness of heavy charged particle beams of helium, carbon, oxygen, neon or argon Bragg peak therapy in the treatment of choroidal melanomas.

II. Establish the nature and incidence of complications utilizing heavy charged particle Bragg peak radiotherapy.

III. Establish the long-term effect of heavy charged particle therapy on visual acuity.

IV. Study the relationship between local control and distant metastatic disease.

PROTOCOL ENTRY CRITERIA: Patients with a diagnosis of small choroidal melanoma demonstrating growth or a growing choroidal melanoma in their only functioning eye and patients who refuse enucleation. Patients must have useful visual potential, no prior radiation therapy and must be able to maintain adequate ocular fixation for safe radiation therapy. Patients must be available for follow-up.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Bragg peak heavy charged particles of helium (cyclotron accelerated), carbon, oxygen, neon, or argon (Bevalac accelerated) encompassing all known tumor with a 1.0 mm margin.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Indirect ophthalmoscopy, ultrasonography, liver function tests, simulation films with diagnostic quality X-ray, immunologic testing with melanoma-associated antigens.

END POINTS: Toxicity/morbidity of treatment, objective tumor response, regression rate, time to disease progression, survival time, overall disease activity.

CURRENT STATUS: At least 25 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

7000 CoRE in 5 fractions over 8 days to the tumor. If needed for tumor control escalate dose in 5% increments after 10 patients are treated at each dose level.

Follow up all patients q month for 6 months, q 3 months for the next 18 months, and q 4 months in the following year.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/79

9.0003 PHASE I/II RADIOTHERAPY WITH FAST NEUTRONS FOR METASTATIC MALIGNANT MELANOMA

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PROTOCOL NUMBER(S) RTOG-8004

OBJECTIVES:

I. Evaluate the response rates of fast neutron beam teletherapy for metastatic malignant melanoma.

II. Determine the degree and rate of tumor regression, the time to onset of local tumor growth (if any), and the rate of regrowth.

III. Determine the time of onset and severity of radiation injury to surrounding normal tissue.

PROTOCOL ENTRY CRITERIA: Patients not more than 75 years of age with histologic evidence of measurable malignant melanoma metastatic or recurrent in the skin, subcutaneous tissues, or peripheral lymphatics. There must have been no prior radiotherapy. The performance status (Karnofsky) must be 50 or greater, and the patient must be able to visit the neutron facility, as well as be available for followup.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Fast neutron beam teletherapy.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Biopsy of lesion, liver scan, lymphangiogram.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 10-30 patients will be entered.

DOSAGE SCHEDULE:

The first 10 patients will be entered in Regimen A. If no adverse normal tissue effects are seen, the next 10 patients will enter Regimen B, and similarly the next 10 enter Regimen C.

Regimen A: 1400 rads in 7 fractions over 4 weeks.

Regimen B: 1600 rads in 8 fractions over 4 weeks.

Regimen C: 1800 rads in 9 fractions over 5 weeks.

All patients will be evaluated monthly for 6 months, then q 2 months for 18 months, then q 3 months through year 5.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 12/80

9.0004 PILOT STUDY OF CHEMOTHERAPY WITH DIBROMODULCITOL (DBD) FOR INCURABLE MALIGNANT MELANOMA

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35294, United States of America

PROTOCOL NUMBER(S) SEG-MEL-P42

OBJECTIVES:

I. Determine response rate and duration of response to dibromodulcitol (DBD) in measurable metastatic malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven malignant melanoma not amenable to surgery or radiotherapy. Patients must be 18 years or older with a Karnofsky performance status of 50 or better and a maximum life expectancy of 6 weeks. Patients must be non-pregnant and have adequate liver and hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dibromodulcitol, DBD, NSC-104800.

STRATIFICATION: Participating institutions, prior therapy.

SPECIAL STUDY PARAMETERS: Brain and liver scans, hepatic and renal function.

END POINTS: Objective tumor response, response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: At least 28 patients to be entered in 12 to 18 months.

DOSAGE SCHEDULE:

DBD - 180 mg/sqm (increase to 220 mg/sqm if no hematologic toxicity appears) po on days 1 through 10. Repeat course q 29 days. Remove patients at the physician's discretion upon relapse or progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DBD - 50 and 100 mg tablets.

DATE SUMMARIZED: 02/80

9.0005 PHASE III RANDOMIZED CONTROLLED ADJUVANT STUDY OF C. PARVUM IMMUNOTHERAPY FOR STAGE I MELANOMA

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35294, United States of America

PROTOCOL NUMBER(S) SEG-77MEL0203; SEG-359; SEG-77MEL313

OBJECTIVES:

I. Determine the effect of C. parvum immunotherapy on the disease-free interval of Stage I melanoma patients who are clinically free of disease and are at a high risk of recurrence.

II. Observe the effect of C. parvum on the survival of these patients.

– III. Serially quantitate the effect of C. parvum on several parameters of cell-mediated and humoral immune functions via recall skin antigens.

PROTOCOL ENTRY CRITERIA: Patients with Stage I non-scalp and non-genitalia melanomas whose lesion has been excised and has invaded to Clark's level III or beyond or exceeds 1.5 mm depth of invasion; previously untreated with anti-tumor agents.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. Corynebacterium parvum (Burroughs-Wellcome), C. parvum, NSC-220537.

Arm II: No therapy (control).

STRATIFICATION BY: Sex, location of lesion, level of invasion, whether a prophylactic regional node dissection was performed, and immunoreactivity to recall skin test antigens.

SPECIAL STUDY PARAMETERS: Recall antigen skin tests.

END POINTS: Disease-free interval, survival, toxicity/morbidity of treatment, immune status.

CURRENT STATUS: Approximately 144 patients will be entered.

DOSAGE SCHEDULE:

Arm I: C. parvum - 1 mg/sqm/extremity sc q 1 week x 12 weeks, then q 2 weeks to relapse or 24 months postoperatively.

Arm II: No treatment.

DOSAGE FORMS: C. parvum - 1.2 ml vials (7 mg/ml).

DATE SUMMARIZED: 05/77

PATIENT ACCRUAL: 00511078

9.0006 PHASE III SURGICAL ADJUVANT IMMUNOTHERAPY WITH CORYNEBACTERIUM PARVUM VS BCG FOR LIMITED STAGE II MELANOMA

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35294, United States of America

PROTOCOL NUMBER(S) SEG-77MEL0303; SEG-77MEL314

OBJECTIVES:

I. Compare the effect of C. parvum and BCG on the disease-free interval of patients with limited Stage II melanoma following surgical removal of all existing disease.

II. Compare the effect of C. parvum and BCG on survival in the same patient population.

III. Quantitate and compare the effect of these regimens on cell-mediated immune functions as measured by serial DNCB skin testing.

PROTOCOL ENTRY CRITERIA: Postoperative Stage II melanoma patients with 4 or less positive regional lymph nodes; previously untreated with chemotherapy, radiation therapy or immunotherapy; selected post-operative Stage I melanomas confined to scalp and genitalia.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. Corynebacterium parvum (Burroughs-Wellcome), C. parvum, NSC-220537.

Arm II: Immunotherapy. BCG-Tice, BCG, NSC-B116341.

STRATIFICATION BY: Sex, clinical stage, pathological stage, number of nodal metastases, location of primary lesion, immunoreactivity to recall skin test antigens.

SPECIAL STUDY PARAMETERS: Serial DNCB skin test reactivity.

END POINTS: Disease-free interval, survival, toxicity/morbidity of treatment, immune status.

CURRENT STATUS: Approximately 190 patients will be entered.

DOSAGE SCHEDULE:

Arm I: C. parvum - 1 mg/sqm/extremity sc q 1 week x 12 weeks, then q 2 weeks to relapse or to 24 months postoperative.

Arm II: BCG - 1 vial divided among axilla and groin node regions by Tine application intradermally q 1 week x 12 weeks, then q 2 weeks to relapse or to 24 months postoperative.

DOSAGE FORMS: C. parvum - 1.2 ml vials (7 mg/ml); BCG - ampules of unspecified weight.

DATE SUMMARIZED: 03/77

9.0007 PHASE III COMPARISON OF DTIC/CTX/C. PARVUM VS C. PARVUM ALONE AS ADJUVANT THERAPY FOR STAGE II-III MELANOMA

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PROTOCOL NUMBER(S) SEG-77MEL0403; SEG-77MEL315

OBJECTIVES:

I. Compare the effectiveness of chemotherapy (DTIC plus cyclophosphamide) plus immunotherapy (Corynebacterium parvum) vs. immunotherapy alone on the 2-year survival of Stage II-III melanoma patients who have had all existing disease removed surgically.

II. Quantitate the effect of these therapeutic regimens on cell-mediated immune functions in this patient population as measured by serial DNCB skin testing.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven Stage II or III melanoma who have had all existing disease removed surgically 1-6 weeks prior to entry. Patients must be between the ages of 14 and 75 years and must have adequate hematologic and liver function. Patients must have a Karnofsky performance status greater than 70 percent and must not have received prior chemotherapy or radiotherapy, except for postoperative brain irradiation for resected cerebral metastases.

PROTOCOL OUTLINE: Randomized study. Enter all patients 1-6 weeks after surgical resection of all existing tumor.

Arm I: 2-Drug Combination Chemotherapy plus Immunotherapy. DTIC, NSC-45388; Cyclophosphamide, CTX, NSC-26271; C. parvum Burroughs-Wellcome, C. parvum B.W., NSC-220537.

Arm II: Immunotherapy. C. parvum B.W.

STRATIFICATION BY: Participating institutions, sex, current pathological stage of disease (II vs. III), prior pathological stage of disease, remission duration, location of primary melanoma, site of metastases, prior immunotherapy (yes vs. no), immunoreactivity to recall skin antigens.

SPECIAL STUDY PARAMETERS: Hematologic parameters; alkaline phosphatase; kidney and liver function tests; chest x-ray; bone, liver, and brain scans; skin tests; DNCB; photographs.

END POINTS: Disease-free interval, survival, recurrence rate.

CURRENT STATUS: 79 patients will be entered in each arm over 2 years.

DOSAGE SCHEDULE:

Arm I: C. parvum B.W. - 4 mg/sqm sc, divided equally among the 4 extremities, repeated weekly for 13 weeks then at 2-week intervals for 2 years or until relapse; DTIC - 600 mg/sqm iv at the start of the third week of Immunotherapy and repeated q 3 weeks for a total of 9 doses; CTX - 600 mg/sqm iv at the start of the third week of Immunotherapy and repeated q 3 weeks for a total of 9 doses.

Arm II: C. parvum B.W. as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: C. parvum B.W. - 8.4 mg vials; DTIC - 100 and 200 mg vials; CTX - 100, 200, and 500 mg vials and 50 mg tablets.

DATE SUMMARIZED: 07/80

9.0008 PHASE III CHEMOTHERAPY WITH BHD (BCNU/DTIC/HU) WITH OR WITHOUT BCG IMMUNOTHERAPY FOR HIGH-RISK MELANOMA PATIENTS

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PROTOCOL NUMBER(S) SWOG-7521

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with BCNU, DTIC and hydroxyurea in preventing recurrence or prolonging survival of patients with resected melanoma who are still at high risk.

II. Determine the effect of adding BCG immunotherapy to combination chemotherapy on disease recurrence and duration of survival of surgically treated melanoma patients.

III. Determine the immune competence of melanoma patients prior to chemo- or immunotherapy and the effect of such therapy on immunocompetence, and correlate with prognosis.

PROTOCOL ENTRY CRITERIA: Patients with histological evidence of melanoma, not more than 4 weeks following removal of localized or nodular lesions, or of locally recurrent or regionally or distant metastasized tumor.

PROTOCOL OUTLINE: Randomized study.

Randomize Class I (localized or nodular lesions) patients to Arms I or II. Randomize Class II (locally recurrent or regionally or distant metastasized tumor) patients to Arms I or III.

Arm I: 3-Drug Combination Chemotherapy. BHD: BCNU, NSC-409962; Hydroxyurea, HU, NSC-32065, Dacarbazine, DTIC, NSC-45388.

Arm II: No treatment (control group).

Arm III: 3-Drug Combination Chemotherapy plus Immunotherapy. Connaught BCG, NSC-B116341. BCNU, HU and DTIC.

STRATIFICATION BY: Disease Class (Class I, localized primary or nodular lesion vs. Class II, regionally recurrent disease or resectable metastatic lesions), age (greater vs. less than 50 years), primary site.

SPECIAL STUDY PARAMETERS: Bone, brain and liver scans; lymphangiography; absolute lymphocyte counts; quantitative immunoglobulins; immunologic competence tests including recall antigens; T and B cell function; lymphocyte transformation.

END POINTS: Duration of disease-free interval, recurrence rate, duration of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: BCNU - 150 mg/sqm iv day 1 and q 56 days thereafter. DTIC - 150 mg/sqm iv daily days 1 through 5 of each course, q 28 days. HU - 1500 mg/sqm po, daily days 1 through 5 of each course q 28 days. Continue treatment for 1 year or until disease recurrence.

Arm II: No treatment.

Arm III: BCNU, HU, and DTIC - as in Arm I. BCG - 600 million cells/dose iv by rotation to each extremity on days 1, 8, and 15 of the month preceding the first course and on days 1, 8, and 15 of the first course of Chemotherapy, then once q 28 days (on day 15 of each course) thereafter for one year.

DOSAGE FORMS: BCNU - 100 mg vials; HU - 500 mg capsules; DTIC - 100 and 200 mg vials.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 02171277

9.0009 PHASE III CHEMOTHERAPY WITH BHD (BCNU/HU/DTIC) AND LEVAMISOLE IMMUNOTHERAPY VS DTIC/ACT-D FOR DISSEMINATED MELANOMA

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PROTOCOL NUMBER(S) SWOG-7727/28

OBJECTIVES:

I. Determine remission induction rates, remission duration, survival and toxicity in patients with disseminated malignant melanoma treated with BCNU, hydroxyurea and DTIC (BHD), BHD plus levamisole, and intermittent single high-dose DTIC plus actinomycin-D in a prospective randomized clinical study.

PROTOCOL ENTRY CRITERIA: Patients with measurable disease of histologically proven disseminated melanoma without prior therapy involving study agents. Patients must have an expected survival time of at least 2 months, must have recovered from toxic effects of prior therapy and must have completed radiotherapy to any bone marrow bearing areas 2 weeks prior to entry. Patients may have renal or hepatic metastases provided liver and kidney functions are adequate.

PROTOCOL OUTLINE: Randomized study on a 1:2:2 basis for Arms I, II and III respectively, and with crossover for nonresponders. Enter patients with brain metastases to Regimen A and patients with hepatic metastases to Regimen B prior to randomization to Arms I, II, or III.

Regimen A: Hormone Therapy plus Radiotherapy. Dexamethasone, DM, NSC-34521; plus brain irradiation.

Regimen B: Single-agent intra-arterial Chemotherapy. DTIC, NSC-45388.

Arm I: 3-Drug Combination Chemotherapy. BHD: BCNU, NSC-409962; Hydroxyurea, HU, NSC-32065; DTIC.

Arm II: 3-Drug Combination Chemotherapy plus Immunotherapy. BCNU, HU, DTIC; plus Levamisole, LEV, NSC-177023.

Arm III: 2-Drug Combination Chemotherapy. DTIC; Actinomycin-D, ACT-D, NSC-3053.

STRATIFICATION BY: Participating institutions; performance status: 0-1 vs. 2-3 vs. 4; age: under 40, 40-59, over 60.

SPECIAL STUDY PARAMETERS: Skin tests according to Protocol SWOG-7475, KLH immunization and other immunologic studies, brain scan.

END POINTS: Objective tumor response, response/remission rate, remission duration, toxicity/morbidity of treatment, survival.

CURRENT STATUS: About 182 patients will be entered in 10 to 12 months.

DOSAGE SCHEDULE:

Regimen A: DM - 8-12 mg/day po for 3 days, then taper to discontinue. On day 3, give Radiotherapy - 4000 rads over a 2-week period to total brain. Enter to Chemotherapy in the second week of Radiotherapy.

Regimen B: Enter patients with massive liver involvement. Cannulate hepatic artery via femoral or brachial artery and give DTIC -200 mg/sqm/day intra-arterially continuously for 5 days. Begin Chemotherapy after 5-7 days.

Arm I: BHD: DTIC - 150 (100 for patients with impaired bone marrow reserve - IMR) mg/sqm/day on days 1 through 5 q 28 days; HU - 1500 mg/sqm/day on days 1 through 5 q 28 days; BCNU - 150 (100 for IMR) mg/sqm on day 1 of q other course on days 1, 57, etc. Delay repeat course until recovery from myelosuppression.

Arm II: BHD - as in Arm I, plus LEV - 2.5 mg/kg on days 6, 7, 13, 14, 20 and 21 of each 28-day course.

Arm III: DTIC - 750 (650 for IMR) mg/sqm iv on day 1 followed by ACT-D - 1.5 (1.25 for IMR) mg/sqm iv on day 1. Repeat course q 3 weeks as tolerated.

Discontinue therapy if disease progresses after 2 courses. Delay therapy if unacceptable toxicity and notify study coordinator. Patients in Arm II or Arm III without response after two courses cross over: Arm II to Arm III, Arm III to Arm II.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; HU - 500 mg capsules; DTIC -100 and 200 mg vials; LEV - 50 mg tablets; ACT-D - 0.5 mg vials.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00940279

9.0010 PHASE II IFOSFAMIDE CHEMOTHERAPY FOR RESISTANT DISSEMINATED MALIGNANT MELANOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7813

OBJECTIVES:

I. Determine the response rate and survival after treatment with ifosfamide in patients with disseminated malignant melanoma who are either ineligible for higher priority studies or who have become resistant to standard therapy or to a higher priority program.

II. Determine the qualitative and quantitative toxicity of ifosfamide in these patients.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed disseminated malignant melanoma not eligible for higher priority protocols or who have failed on standard regimens or higher priority programs. Patients must have normal kidney and hematologic function, no chronic renal disease and no history of hemorrhagic cystitis from prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

– Single-agent Chemotherapy plus supportive Vitamin Therapy. Ifosfamide, IPP, NSC-109724; Ascorbic Acid, VIT-C, NSC-33832.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Urinalysis for hematuria.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response, response duration, survival time.

CURRENT STATUS: 21 patients will be entered.

DOSAGE SCHEDULE:

IPP - 1.2 mg/sqm iv 30 min infusion on days 1 through 5 q 3 weeks. Give adequate hydration and VIT-C - 500 mg 3x/day on days of IPP administration. Do not repeat therapy until no more than 10 rbc are present/HPF of urine sample. Give a minimum of 2 courses. Remove from study patients with increasing disease, unacceptable toxicity or patients in complete remission who have received 2 years of therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: IPP - 1 and 3 gm vials.

DATE SUMMARIZED: 12/79

9.0011 PHASE II PILOT CHEMOTHERAPY WITH VINDESINE IN ADULTS WITH METASTATIC MALIGNANT MELANOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7930

OBJECTIVES:

I. Determine the efficacy based on response rate and duration of desacetyl vinblastine amide sulfate (vindesine) in adults with metastatic malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable and metastatic malignant melanoma. Initial granulocyte count of 2000/cumm and platelet count of 100,000/cumm or greater are required. There must be a life expectancy of at least 6 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Neurologic evaluation.

END POINTS: Toxicity/morbidity of treatment, survival rate, response rate and duration, response/remission rate.

CURRENT STATUS: A minimum of 25 evaluable patients will be entered; 50% of the patients will be untreated.

DOSAGE SCHEDULE:

DAVA - 3 mg/sqm iv at 7-day intervals as tolerated. Subsequent doses given only when blood count reaches nadir and recovery is evident: WBC greater than 3,000, absolute granulocyte greater than 1, 500 and platelet count greater than 100,000. At 1- or 2-week intervals (tolerance dependent), dose is increased to 4 mg/sqm, then to 5 mg/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DAVA - 5 mg ampules.

DATE SUMMARIZED: 02/80

9.0012 PHASE II PILOT CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE FOR ADULT METASTATIC MALIGNANT MELANOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-8065

OBJECTIVES:

I. Determine the activity, as measured by response rate and duration of response, of dihydroxyanthracenedione (DHAD) in a single dose every-three-week schedule in adults with metastatic malignant melanoma.

II. Define the qualitative and quantitative toxicities of DHAD administered in a Phase II study.

PROTOCOL ENTRY CRITERIA: Adult patients with histologically confirmed advanced malignant melanoma with a measurable lesion. A life expectancy of at least 6 weeks and a Karnofsky performance status of 30-40 or better are required. Patients must not be eligible for protocols of higher priority or therapy of higher efficacy. Prior chemotherapy must have beeen terminated for 3 weeks (6 weeks for nitrosoureas) and patients must have recovered from the toxic effects of any prior therapy. Patients must have a pretreatment WBC of 3500/cumm or greater, a platelet count of 125,000/cumm or greater, and serum creatinine and bilirubin of 2.0 mg percent or less.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Participating institutions; prior chemotherapy: yes vs. no.

SPECIAL STUDY PARAMETERS: Fasting blood sugar, EKG, CAT, x-ray, pharmacokinetic studies, lumbar puncture, CBC and platelets, renal and hepatic function tests, tumor measurements.

END POINTS: Response/remission rate, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 14 patients will be entered in 6 months; a total of 25 patients will be entered, if responses are observed.

DOSAGE SCHEDULE:

DHAD - 12 mg/sqm through a running iv over 30 minutes q 3 weeks, provided patient has recovered from previous drug-induced toxicity. Patients who show disease progression or unacceptable stable disease after 2 courses go off study. Those who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 5 mg ampules.

DATE SUMMARIZED: 10/80

9.0013 PHASE III ADJUVANT CHEMOTHERAPY WITH DTIC VS CHEMOIMMUNOTHERAPY WITH DTIC/MER IN STAGE III/IV MALIGNANT MELANOMA

Lichtenfeld, J. L., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7411

OBJECTIVES:

I. Determine the efficacy of DTIC as adjuvant therapy in patients with Stage III-IV malignant melanoma in whom all gross disease has been resected.

II. Determine the efficacy of combined DTIC/MER-BCG in the treatment of patients with advanced nonresectable malignant melanoma.

III. Evaluate patient tolerance to a q-10-day MER-BCG administration schedule.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage III or Stage IV malignant melanoma whose estimated survival is not less than 3 weeks. Patients may have received treatment with neither DTIC nor any immunotherapeutic agent prior to entry.

PROTOCOL OUTLINE: Randomized study. Randomize all patients in whom all detectable disease has been resected (Group A) to Arms I and II. Randomize all patients with suspected residual disease but no measurable disease (Group B) and all patients with measurable and nonresectable disease (Group C) to Arms II and III.

Arm I: Single-agent Chemotherapy. DTIC, NSC-45388.

Arm II: No treatment.

Arm III: Single-agent Chemotherapy plus Immunotherapy. DTIC; MER-BCG, MER, NSC-143769.

STRATIFICATION BY: Residual disease (present vs. not present).

SPECIAL STUDY PARAMETERS: Hemogram, blood chemistries, skin tests, appropriate scans, chest x-rays, tumor measurements.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: DTIC - 250 mg/sqm iv infusion over 45 minutes on days 1 through 5. Repeat course q 21 days for a total of 6 courses. Enter failures during treatment or within 4 weeks after completing treatment to Arm IV. Randomize patients failing more than 4 weeks after the last course of DTIC to Arm III or further courses of Arm I, but not as a part of this study. Group C patients continue treatment q 6 weeks for an additional 6 courses; they then continue treatment q 12 weeks until failure. Failures enter Arm III.

Arm II: No treatment. Enter failures to Arm III and evaluate as a part of this study.

Arm III: DTIC - 250 mg/sqm iv infusion over 45 minutes on days 1 through 5; MER - 2 mg in 1 ml administered into 5 intradermal sites on days 7 and 17. Repeat course q 21 days for a total of six courses, then q 6 weeks for an additional 6 courses. Group C patients continue treatment q 12 weeks until failure. Treat Group B and Group C failures with alternative Chemotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/80

9.0014 PHASE II EVALUATION OF AMSA IN PATIENTS WITH ADVANCED STAGE III/IV MALIGNANT MELANOMA

Fuks, J., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7913

OBJECTIVES:

I. Determine the therapeutic efficacy of AMSA in the treatment of patients with Stage III/IV malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage III or Stage IV malignant melanoma whose minimum expected survival is greater than 3 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-6, SMA-12, clotting studies, EKG, chest x-ray or whole-lung tomograms, scans as indicated, bone marrow biopsy in cases of prior tumor involvement, UGI.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 20 patients will be required in the first 12 months. If there is evidence of clinical responsiveness, an additional 10-30 patients will be required in the second 12 months.

DOSAGE SCHEDULE:

AMSA - 150 mg/sqm iv over 60 minutes q 21 days. In the absence of hematologic toxicity, increase subsequent doses by 30 mg/sqm. Give a minimum of 3 courses of therapy, and continue responders on treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

9.0015 EVALUATION OF DAVA FOR ANTITUMOR ACTIVITY IN PATIENTS WITH METASTATIC MELANOMA

Ostrow, S., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7916

OBJECTIVES:

I. Determine whether vindesine has therapeutic value in patients with metastatic melanoma.

II. Determine the toxicity of vindesine in patients with metastatic melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented melanoma whose disease is metastatic and not amenable to surgery. Patients must have measurable disease, adequate marrow function, and normal renal and hepatic function. There must be no history of another primary neoplasm.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Chest x-rays with whole-lung tomograms and metastatic bone survey as indicated, isotopic scanning as indicated, hematologic parameters, liver and kidney function tests, CEA, EKG, serum proteins, electrolytes.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, duration of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

DAVA - 3 mg/sqm/week iv for 6 doses, then q 2 weeks. Minimum treatment will be for 8 weeks, with responders continuing treatment until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

9.0016 PHASE II COMBINATION CHEMOTHERAPY WITH DBD/MECCNU FOR ADVANCED MALIGNANT MELANOMA

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-797003

OBJECTIVES:

I. Conduct a Phase II evaluation of the combination dibromodulcitol/methyl-CCNU in patients with advanced malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven malignant melanoma with measurable or evaluable metastatic disease that is incurable by surgery or radiation or is progressing following previous treatment. Patients must have an ECOG performance score less than 4 and adequate hematologic, renal, and hepatic function. Patients must not undergo major surgery within the 3 weeks prior to entry or be treated with chemotherapy within 4 weeks prior to entry (6 weeks for mitomycin-C or nitrosoureas). Patients must not have had radiotherapy in excess of 3000 rads to more than 30 percent of the bone marrow.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Dibromodulcitol, DBD, NSC-104800; Methyl-CCNU, MeCCNU, NSC-95441.

STRATIFICATION BY: Performance score: 0-1 vs. 2-3; dominant disease: visceral vs. nonvisceral; measurable disease vs. evaluable disease.

SPECIAL STUDY PARAMETERS: Tumor measurements; chest x-ray; hematologic, renal, and liver function tests.

END POINTS: Response/remission rate, objective tumor response, duration of response, survival.

CURRENT STATUS: Initially 14 previously treated patients will be entered. If there are any regressions in these patients, 14 or 20 previously untreated patients will be entered. Patients will be accrued over a 12- to 18-month period.

DOSAGE SCHEDULE:

DBD - 60 mg/sqm po daily; MeCCNU - 135 mg/sqm po on day 1 q 6 weeks. Patients are treated until progression. Radiation therapy may be given to patients who develop CNS metastases.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DBD - 50 mg tablets; MeCCNU - 10, 50, and 100 mg capsules.

DATE SUMMARIZED: 10/80

9.0017 PHASE II CHEMOTHERAPY WITH VINBLASTINE/BLEOMYCIN/CIS-PLATINUM IN PATIENTS WITH DISSEMINATED MALIGNANT MELANOMA

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-807001

OBJECTIVES:

I. Evaluate in a Phase II study the effectiveness of vinblastine/bleomycin/cis-platinum in patients with advanced malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven malignant melanoma who have measurable or evaluable metastatic disease that is incurable by surgery or radiation at the time of diagnosis or following progression of disease after previous treatment for any stage of disease. Patients may not have had prior chemotherapy and must have adequate hematologic and pulmonary function. The ECOG performance score must be better than 4. There may have been no prior surgery within 3 weeks and no prior or concomitant radiation therapy to greater than 30 percent of the bone marrow.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Induction.

3-Drug Combination Chemotherapy. Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

Regimen B: Maintenance.

2-Drug Combination Chemotherapy. VBL; CACP. STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic parameters, chest x-ray.

END POINTS: Response rate, duration of response, interval to progression, survival.

CURRENT STATUS: The estimated duration of accrual for the study is 12-18 months.

DOSAGE SCHEDULE:

Regimen A: VBL - 6 mg/sqm iv push on days 1 and 2; BLEO - 15 U/sqm/day by continuous 24-hour iv infusion on days 1 through 5 (total dose of BLEO restricted to 300 U/sqm and the maximum dose 500 U over 4 monthly courses); CACP - 50 mg/sqm iv with forced diuresis on day 5. Course repeated q 4 weeks for a total of 4 courses.

Regimen B: VBL - 6 mg/sqm iv push on days 1 and 2; CACP - 50 mg/sqm with forced diuresis on day 2. Course repeated q 4 weeks. Patients who progress at any time will go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VBL - 10 mg vials; BLEO - 15 U ampules; CACP - 10 mg vials.

DATE SUMMARIZED: 07/80

9.0018 PHASE II CHEMOTHERAPY WITH L-ALANOSINE FOR ADVANCED MALIGNANT MELANOMA

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-807003

OBJECTIVES:

I. Assess the antitumor activity and toxicity of L-alanosine in patients with advanced malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven malignant melanoma, measurable or evaluable metastatic disease that is incurable by surgery or radiotherapy at the time of entry. Patients who have received previous treatment for any stage of disease must show objective and/or subjective progression of disease. Patients must have an ECOG performance status better than 4; there must be adequate renal function (creatinine greater than 1.9 mg/dl). There must be no clinically significant cardiovascular disease. Patients must have received no prior treatment with L-alanosine at any time and no prior chemotherapy within the 3 weeks prior to entry (6 weeks for nitrosoureas).

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. L-Alanosine, NSC-153353.

STRATIFICATION BY: None

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic, renal and hepatic function tests; chest x-ray; EKG.

END POINTS: Response/remission rate, objective tumor response, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 26-39 patients will be entered.

DOSAGE SCHEDULE:

L-Alanosine - 250 mg/sqm iv over a 10-minute period on days 1 through 3 q 3 weeks. Patients are evaluated after 1 course; patients who are stable, improved, or in regression continue on study. Patients with progressive disease go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: L-Alanosine - 100 mg vials.

DATE SUMMARIZED: 01/81

9.0019 ADJUVANT CHEMOIMMUNOTHERAPY WITH DTIC, ACTINOMYCIN-D AND C. PARVUM FOR STAGE IIIB OR IIIAB MALIGNANT MELANOMA

Gutterman, J. U., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-192; MDA-DT-7659

OBJECTIVES:

I. Evaluate the efficacy of chemotherapy with actinomycin-D and DTIC plus immunotherapy with C. parvum in prolonging the postoperative disease-free interval and survival of patients with Stage IIIB or IIIAB melanoma.

PROTOCOL ENTRY CRITERIA: Patients with melanoma metastatic to regional lymph nodes (Stages IIIB or IIIAB) who have had no prior therapy with actinomycin-D, DTIC or C. parvum, and who have adequate bone marrow, liver and renal functions.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy plus 2-Drug Combination Chemotherapy. C. parvum, NSC-220537; Actinomycin-D, ACT-D, NSC-3053; DTIC, NSC-45388.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 75 patients will be entered per year.

DOSAGE SCHEDULE:

Immunotherapy. High-dose regimen for patients under 60 years of age. C. parvum - 0.25 mg/sqm iv on days 1 and 2; 0.5 mg/sqm iv on day 3; 1.0 mg/sqm iv on day 4; 2.0 mg/sqm iv on days 5 through 14. Low-dose regimen for patients over 60 years of age. C. parvum - 0.2 mg/sqm/day for 14 days. At completion of iv Immunotherapy, begin Chemotherapy plus id Immunotherapy. ACT-D - 1.5 mg/sqm iv on day 1; DTIC - 250 mg/sqm iv on days 1 through 5; C. parvum - 2 mg/sqm id on days 7, 12 and 17, rotating to upper arms and legs. Repeat Chemotherapy plus id C. parvum cycle q 21 days, blood count permitting, adding iv C. parvum regimen every 3 cycles.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/77

9.0020 CHEMOTHERAPY WITH CIS-PLATINUM WITH OR WITHOUT ACTINOMYCIN-D FOR REGIONALLY CONFINED MELANOMA

Benjamin, R. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-252; MDA-DT-7760

OBJECTIVES:

I. Determine the antitumor efficacy of cis-platinum alone or in combination with actinomycin D when administered by intra-arterial infusion.

II. Study the pharmacology of these agents.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed melanoma confined to an area supplied by an artery which can be catheterized.

PROTOCOL OUTLINE: Nonrandomized study. Enter all patients to Regimen A; if no improvement cross over to Regimen B.

Regimen A: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Regimen B: 2-Drug Combination Chemotherapy. CACP; Actinomycin-D, ACT-D, NSC-3053.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, objective tumor response.

CURRENT STATUS: About 25 patients will be entered in 1 1/2 years.

DOSAGE SCHEDULE:

Regimen A: CACP - 150 mg/sqm intra-arterially (ia) by catheterization, with adequate hydration.

Regimen B: CACP - 80 mg/sqm by ia catherization; ACT-D - 1.5 mg/sqm by ia catheterization; both with adequate hydration. Frequency and duration of therapy are not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

9.0021 CHEMOTHERAPY WITH HIGH-DOSE CIS-PLATINUM FOR DISSEMINATED MALIGNANT MELANOMA

Plager, C., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-299; MDA-M/gm38

OBJECTIVES:

I. Determine the efficacy of high-dose cis-platinum in the treatment of disseminated (MDAH Stage IV) malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients over the age of 16 with histologically confirmed malignant melanoma, with disseminated disease, measurable lesions and measurable metastases. Patients must have failed chemotherapy regimens of higher priority. Patients must have a life expectancy of at least 2 months and there must be adequate bone marrow function and creatinine clearance. There must be no evidence of obstructive uropathy or serious cardiac or pulmonary disease; hearing function must be acceptable. Patients must be off all previous chemotherapy, radiotherapy and immunotherapy for at least 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests, serum electrolytes, glucose, uric acid, calcium, magnesium, urine electrolytes, SMA-12, audiogram, creatinine clearance, EKG.

END POINTS: Response/remission rate, disease-free interval, objective tumor response, duration of response.

CURRENT STATUS: A minimum of 25 patients will be required.

DOSAGE SCHEDULE:

CACP - 100 mg/sqm iv infusion over 15 to 30 minutes. If no severe hematologic, renal and ototoxicity results, the dose will be increased to 125 mg/sqm for subsequent courses. Repeat q 3-4 weeks or longer as hematologic, renal and ototoxicity necessitate. Patients who show progressive disease after 2 courses and those who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

9.0022 CIS-PLATINUM CHEMOTHERAPY PLUS CRANIAL RADIOTHERAPY FOR MELANOMA WITH CNS INVOLVEMENT

Stewart, D. J., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-330; MDA-DT-7904

OBJECTIVES:

I. Determine the efficacy of cis-platinum (CACP) with cranial irradiation in the treatment of Stage IV malignant melanoma, with intracranial metastasis with or without extracranial disease.

II. Determine the qualitative and quantitative toxicity of CACP and cranial irradiation and the duration of response and survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with histological proof of disseminated malignant melanoma, with evidence of intracerebral metastasis by CAT or brain scan. Patients may have undergone partial resection of intracerebral tumor and must have evaluable intracerebral lesion, and they may also have extracranial disease. Patients must have adequate bone marrow, liver and renal function and must have terminated all prior therapy 4 weeks prior to entry, with recovery from toxic effects.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Radiotherapy. cis-Platinum, CACP, NSC-119875; plus cranial irradiation.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: CAT or brain scan.

END POINTS: Toxicity/morbidity of treatment, response duration, response/remission rate, survival time, objective tumor response.

CURRENT STATUS: 35 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

3000 rad in 12 fractions given in 16 days to the entire cranial cavity; plus CACP - 40 mg/sqm (route not given) given on days 1, 8 and 15 during cranial radiation and preferably less than 4 hours prior to radiotherapy, then given 120 mg/sqm q 3 to 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/79

9.0023 IMMUNOTHERAPY WITH BCG VS INTERFERON FOR STAGE IIIB RECURRENT MELANOMA OF TRUNK, HEAD, OR NECK

Gutterman, J. U., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-337; MDA-DT-7924

OBJECTIVES:

I. Compare the efficacy of immunotherapy with BCG vs. interferon as adjuvant treatment following surgery for malignant melanoma of trunk, head, or neck metastatic to regional lymph nodes.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed malignant melanoma of the trunk, head, or neck region metastatic to regional lymph nodes (Stage IIIB) who have had surgical removal of tumor involved lymph nodes. Patients must have adequate bone marrow, liver and kidney function and must not have had prior exposure to protocol agents.

PROTOCOL OUTLINE: Randomized study.

Arm I. Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: Immunotherapy. Human leucocyte Interferon, Interferon.

STRATIFICATION: Participating institutions; nodal involvement: less than 5 vs. more than 5; site of primary: trunk vs. extremities vs. head and neck; site of surgery: M.D. Anderson vs. other.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, survival time, disease-free survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: BCG - 6 x 10 to the eighth viable units by scarification q week for 3 months, than q other week for a total of 12 months.

Arm II: Interferon - 3 million units/day im for 56 days, then 3 times a week for a total of 12 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

9.0024 PHASE II CHEMOTHERAPY WITH CONTINUOUS VINDESINE INFUSION FOR STAGE IV METASTATIC MELANOMA

Yap, B. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-349; MDA-DT-7943

OBJECTIVES:

I. Determine the efficacy in terms of response rate and survival of continuous 5-day infusion of vindesine in patients with disseminated melanoma and the qualitative and quantitative toxicity of vindesine administered in this fashion.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with measurable lesions of Stage IV metastatic melanoma not eligible for higher priority protocols. Patients must have a life expectancy of at least 12 weeks, and they must have adequate bone marrow, liver and renal function unless this therapy is indicated as a life-saving measure. They must have terminated all prior therapy 4 weeks before study entry and have recovered from any toxic effects.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival time, objective tumor response.

CURRENT STATUS: A minimum number of 25 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 1.2 mg/sqm (1 mg/sqm for patients with inadequate bone marrow and abnormal liver function) continuous 24-hour iv infusion on days 1 through 5 q 21 days. A minimum of 2 courses is considered an adequate trial.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

9.0025 PHASE II CHEMOTHERAPY WITH CACP VS CACP/ARA-C FOR DISSEMINATED MALIGNANT MELANOMA

Latreille, J., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-380; MDA-DT-7983

OBJECTIVES:

I. Determine the efficacy of cis-platinum (CACP) alone or in combination with cytosine arabinoside (ARA-C) in patients with metastatic malignant melanoma.

II. Determine the qualitative and quantitative toxicity of this combination chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented malignant melanoma not eligible for front line chemotherapy. Patients must have measurable lesions and a life expectancy of at least 3 months. Patients must be off prior radiotherapy and/or chemotherapy for at least 4 weeks prior to entry. Patients who have failed on prior combinations including cis-platinum or ARA-C are eligible for the combined regimen only. Bone marrow, liver, and renal function must be adequate.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: 2-Drug Combination Chemotherapy. CACP; Cytosine arabinoside, ARA-C, NSC-63878.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response, survival rate.

CURRENT STATUS: A minimum of 15 patients on both arms will be entered.

DOSAGE SCHEDULE:

Arm I: CACP - 100 mg/sqm iv infusion. The starting dose will be reduced by 1 level if the patient showed severe myelosuppression in the past or had been treated with nitrosoureas and/or Mitomycin-C.

Arm II: ÇACP as in Arm I; ARA-C - 500 mg/sqm iv infusion over 20 minutes following CACP infusion.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

9.0026 PHASE II CHEMOTHERAPY WITH VINDESINE INFUSION PLUS DTIC FOR STAGE IV METASTATIC MALIGNANT MELANOMA

Yap, B. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-382; MDA-DT-7996

OBJECTIVES:

I. Determine the therapeutic efficacy of continuous 5-day infusions of vindesine combined with DTIC in patients with disseminated malignant melanoma.

II. Determine the quantitative and qualitative toxicity of this combination chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven Stage IV metastatic malignant melanoma who have not previously been treated with 5-day infusions of vindesine or single doses of DTIC. Patients must have a life expectancy of at least 12 weeks, must have measurable lesions, and must be off all previous chemotherapy, immunotherapy, or radiotherapy for the 4 weeks prior to entering. Patients must be at least 15 years old and have adequate bone marrow, renal, and hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. DTIC, NSC-45388; Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: A minimum of 25 patients is required for statistical validity.

DOSAGE SCHEDULE:

DTIC - 800 mg/sqm on day 1; DAVA - 1 mg/sqm/day for 5 days by continuous 24-hour/day infusion. Courses repeated q 3 weeks depending on recovery from myelosuppression or other toxicities.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

9.0027 PHASE II COMBINATION CHEMOTHERAPY WITH DAVA/DTIC PLUS MER IMMUNOTHERAPY FOR STAGE IV METASTATIC MALIGNANT MELANOMA

Yap, B. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-382R; MDA-DT-7996R

OBJECTIVES:

I. Determine the therapeutic efficacy of continuous 5-day infusion of vindesine combined with DTIC in patients with disseminated malignant melanoma.

II. Determine the qualitative and quantitative toxicity of this combination chemotherapy.

III. Determine whether the intravenous administration of MER-BCG adds to the response rate or duration of response achieved with chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with histologic proof of Stage IV metastatic malignant melanoma with measurable lesions. Patients must have a life expectancy of at least 12 weeks; bone marrow, liver, and renal function must be adequate (unless this therapy is indicated as a life-saving measure). Patients must have been off all chemotherapy, immunotherapy, or radiotherapy for the 4 weeks prior to entry and must have had no previous therapy with vindesine or DTIC given on the protocol schedule.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy plus Single-agent Immunotherapy. Dacarbazine, DTIC, NSC-45388; Vindesine, DAVA, NSC-245467; plus MER-BCG, MER, NSC-143769.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function tests.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 50 evaluable patients will be entered.

DOSAGE SCHEDULE:

DTIC - 800 mg/sqm iv on day 1; DAVA - 1.0 mg/sqm iv continuous 24-hour infusion via a central venous catheter on days 1-5; plus MER - 0.5 mg/sqm iv over 1 hour via the central iv line or a peripheral iv line on days 7 and 14. (Patients with prior BCG, prior tuberculosis or a positive intermediate PPD skin test receive 0.05 mg/sqm MER.) Course is repeated q 3 weeks depending upon recovery from myelosuppression or other toxicities. A minimum of 2 courses is required for an adequate trial.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

9.0028 PHASE II CHEMOTHERAPY WITH AZQ FOR STAGE IV METASTATIC MALIGNANT MELANOMA

Yap, B. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-392; MDA-DT-8024

OBJECTIVES:

I. Determine the therapeutic efficacy in terms of response rate and survival of AZQ administered by 5-day intravenous infusion in patients with metastatic malignant melanoma.

II. Determine the qualitative and quantitative toxicity of AZQ administered in this fashion.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic melanoma with measurable lesions. Patients must be at least 15 years of age; they must have a life expectancy of at least 12 weeks, and have adequate bone marrow, liver, and renal function. Patients may not receive therapy for four weeks prior to entry and must have recovered from any toxic effects of previous therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. AZQ, NSC-182986.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic function tests.

END POINTS: Response/remission rate, objective tumor response, duration of response, disease-free interval, length of survival, survival rate.

CURRENT STATUS: A minimum of 30 patients will be entered.

DOSAGE SCHEDULE:

AZQ - 8 mg/sqm (in good-risk patients with adequate bone marrow reserve and no prior Mitomycin-C or Nitrosourea therapy) iv daily for 5 days q 4 weeks, with increments of 2 mg/sqm based on granulocyte and platelet counts. Poor-risk patients (inadequate bone marrow reserve, prior mitomycin-C or nitrosourea chemotherapy, or radiotherapy to the chest, spine, or pelvis) receive an initial dose of 6 mg/sqm. All patients receive at least 2 courses. Chemotherapy is continued for 2 years or for 1 year after achieving CR, whichever is shorter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/80

9.0029 PCNU PLUS CRANIAL IRRADIATION IN THE TREATMENT OF PATIENTS WITH STAGE IV MALIGNANT MELANOMA WITH CNS METASTASES

Feun, L. G., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-429; MDA-DT-8055

OBJECTIVES:

I. Determine the therapeutic efficacy of combining PCNU with cranial irradiation in the treatment of patients with Stage IV melanoma with intracranial metastases with or without extracranial diseases.

PROTOCOL ENTRY CRITERIA: Patients over the age of 15 with histologically documented disseminated malignant melanoma with evidence of intracerebral metastases whether or not they have extracerebral metastases. Patients who have had previous cranial irradiation are eligible for PCNU alone, but patients may not have been previously treated with PCNU. Patients may have had previous partial resection of metastases. There should be evaluable lesions on the brain scan or on the CT scan, or both. Patients should not have received radiotherapy or chemotherapy during the 3 weeks prior to entry. Bone marrow, hepatic, and renal function should be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Single-agent Chemotherapy. PCNU, NSC-95466.

Regimen B: Radiotherapy.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment, objective tumor measurements.

CURRENT STATUS: At least 35 evaluable patients will be entered.

DOSAGE SCHEDULE:

Regimen A: PCNU - 90 mg/sqm iv q 6-8 weeks, the first dose to be administered within 24 hours of starting Regimen B. Escalate to 110 mg/sqm if WBC nadir was more than 2000 and platelet nadir was more than 100,000. In order to be evaluable, patients must receive at least 2 courses.

Regimen B: 3000 rads to the midline of the brain in 10 daily fractions of 300 rads. Begin within 24 hours of the first dose of PCNU.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

9.0030 PHASE II CHEMOTHERAPY WITH INTRA-ARTERIAL CACP AND DTIC FOR REGIONALLY CONFINED METASTATIC MALIGNANT MELANOMA

Calvo, D. B., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-430; MDA-DT-8053

OBJECTIVES:

I. Determine the antitumor activity and toxicity of cis-platinum and DTIC administered intra-arterially in patients with regionally confined metastatic malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented disseminated melanoma confined to a region supplied by an artery that can be catheterized. Patients may not have received either study drug prior to entry and must be off all chemotherapy, immunotherapy, and radiotherapy for at least 4 weeks prior to entry. Patients must be at least 15 years old and have measurable disease. Bone marrow, renal, and cardiovascular function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. DTIC, NSC-45388; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, survival.

CURRENT STATUS: About 20 patients will be required.

DOSAGE SCHEDULE:

DTIC - 800 mg/sqm ia over 2-3 hours, with second-dose escalation to 900 mg/sqm if granulocyte nadir was not less than 2000 and platelet nadir was not less than 100,000; CACP - 90 mg/sqm ia over 2-3 hours with no escalation on subsequent doses. If after 2 courses there is no response, patient will be removed from study. Patients who are stable or have PR or CR after 2 courses will receive an additional course and then be evaluated for resection or biopsy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

9.0031 CHEMOTHERAPY WITH ACT-D/DTIC WITH OR WITHOUT IMMUNOTHERAPY WITH C. PARVUM FOLLOWING CURATIVE RESECTION OF METASTATIC MELANOMA

Gutterman, J. U., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-74; MDA-DT-7602, MDA-DT-7602A

OBJECTIVES:

I. Determine the efficacy of the combination of DTIC and actinomycin-D with or without intravenous Corynebacterium parvum in metastatic melanoma.

II. Determine the pharmacologic effects of iv C. parvum on DTIC metabolism.

III. Determine the qualitative and quantitative toxicity of daily C. parvum combined with DTIC and actinomycin-D.

PROTOCOL ENTRY CRITERIA: Patients who have had total surgical removal of histologically proven, measurable lesions of metastatic malignant melanoma, Stage IVA or IVB. Patients must have had no prior therapy with any agents used in this study and must have adequate liver, kidney and bone marrow functions.

PROTOCOL OUTLINE: Randomized study (as revised MDA-DT-7602A).

Arm I: 2-Drug Combination Chemotherapy plus Immunotherapy. DTIC, NSC-45388; Actinomycin-D, ACT-D, NSC-3053; plus Corynebacterium parvum, C. parvum, NSC-220537.

Arm II: 2-Drug Combination Chemotherapy. DTIC; ACT-D.

STRATIFICATION BY: Participating institutions; age; disease stage.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response.

CURRENT STATUS: 100 patients will be entered.

DOSAGE SCHEDULE:

Arm I: C. parvum - begin 14 days prior to Chemotherapy - 0.25 mg/sqm iv on days 1 and 2, .5 mg/sqm iv on day 3, 1 mg/sqm iv on days 4, 2 mg/sqm on days 5 through 14, and on days 21 and 28; DTIC - 250 mg/sqm/day iv on days 15 through 19; ACT-D - 2 mg/sqm iv on day 15. Repeat day 15 through 36 therapy q 3 weeks, if blood counts permit, for 3 complete cycles, then re-intensify with 14 days of C. parvum therapy. Repeat Re-intensification after q 3 courses.

Arm II: DTIC, ACT-D, as in Arm I.

Remove from study patients with increasing disease after two courses or patients with unacceptable status quo or toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DTIC - 100 and 200 mg ampules; ACT-D - 0.5 mg vials; C. parvum - 7 mg/ml formalin-killed C. parvum suspension vials.

DATE SUMMARIZED: 01/79

9.0032 IMMUNOTHERAPY WITH NEURAMINIDASE-TREATED MELANOMA CELLS AND BCG VS BCG ALONE VS CHEMOTHERAPY WITH MECCNU FOR OPERABLE MELANOMA

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PROTOCOL NUMBER(S) NCI-76-C-151; NCI-IB-2

OBJECTIVES:

I. Compare surgery alone vs. treatment with neuraminidase-digested allogeneic tissue culture melanoma cells plus BCG following surgery vs. treatment with BCG alone following surgery vs. chemotherapy with methyl CCNU following surgery for Stage I and II melanoma.

PROTOCOL ENTRY CRITERIA: Patients with: Stage I melanoma where the primary was cutaneous and of Clark level IV (thickness greater than 2.25 mm) or of Clark level V; Stage I local recurrence within 5 cm of the primary; Stage II melanoma including Stage II with local recurrence within 5 cm of the primary. All Stage II patients must have had a primary cutaneous lesion and histologically positive metastatic disease in lymph nodes. All patients must have had a wide excision of the primary lesion with regional lymph node dissection no more than 6 months prior to entry. Patients must be between 15 and 70 years of age and have adequate renal and hepatic function. Patients must not have: concomitant severe disease; primary lesions in the eye, on mucous membranes, soles or palms; an unknown primary site; or history of other malignant diseases (except basal cell carcinoma). Patients must not have received chemotherapy for 2 months prior to entry.

PROTOCOL OUTLINE: Randomized study. Patients are randomized following surgery.

Arm I: Combination Immunotherapy. BCG-Trudeau Institute plus Neuraminidase-treated allogeneic tumor cells, NAC, plus Mitomycin-treated and Neuraminidase-treated allogeneic tumor cells, M-NAC.

Arm II: Single-agent Immunotherapy. BCG-Trudeau Institute.

Arm III: Single-agent Chemotherapy. Methyl CCNU, MeCCNU, NSC-95441.

Arm IV: No further treatment.

STRATIFICATION BY: Disease stage: Stage I, level IV, thickness greater than 2.25 mm vs. Stage I, level V, vs. Stage I (any level) with local recurrence vs. Stage II vs. Stage II with local recurrence; site of primary: head, neck or trunk vs. extremities; number of histologically positive nodes (in Stage II patients only): 1, 2 vs. 3 or more; histologic status (in Stage II patients only): positive vs. negative.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; anti-HL-A titer of serum; cytotoxic antibody; cellular cytotoxicity; antibody-dependent cell-mediated cytotoxicity; KLH-titer; chest x-ray; skin tests and immunizations: PPD, Candida, SKSD, Trichophyton.

END POINTS: Recurrence rate, length of survival, disease-free interval, survival rate.

CURRENT STATUS: 150 patients have been entered; an additional 50 will be required.

DOSAGE SCHEDULE:

Treatment is given at weekly intervals, beginning no sooner than 10 days postoperatively.

Arm I: Week 1: M-NAC - 2 x 10 to the 8th cells mixed with BCG - 5 x 10 to the 5th organisms administered in 20 equally divided id injections at four 16-sqm area sites: both lateral chest walls and both abdominal walls; repeat in one week. Week 3: M-NAC - 2 x 10 to the 8th cells id as in week 1 followed by BCG - 4.2 x 10 to the 8th organisms id via 15 strokes of the Heaf gun at week 1 sites; repeat in one week. Week 5: NAC - 2 x 10 to the 7th cells id via 15 strokes of the Heaf gun; repeat in one week. Weeks 7 through 11: NAC - 5 x 10 to the 7th cells Heaf gun id injection at week 1 sites. Beginning week 12, NAC plus BCG as per week 3 q other week for two years.

Arm II: BCG - 1 x 10 to the 6th organisms id at sites as per Arm I; repeat in one week. Beginning week 3, BCG - 4 x 10 to the 8th organisms id via Heaf gun, q week for a total of 10 immunizations. Beginning with week 14, BCG - 4 x 10 to the 8th organisms id (Heaf gun) q other week for 2 years.

Arm III: MeCCNU - 200 mg/sqm po, q 6 weeks if blood counts have recovered.

Arm IV: Observation only following surgery.

All patients are assessed in clinical and immunological followup q 30 days for 3 months, at 6 months, then q 3 months thereafter indefinitely or until recurrence or progression of disease. Patients who have local recurrence, have in-transit metastases, develop systemic BCG infection, or exhibit growth of the allogeneic cells at immunization sites go off study. Patients with Stage I disease that progresses to Stage II or Stage III and patients with Stage II disease that progresses to Stage III go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MeCCNU - 50 and 100 mg capsules; BCG - 5 x 10 to the 8th viable organisms per vial.

DATE SUMMARIZED: 08/80

9.0033 IMMUNOTHERAPY WITH BCG WITH OR WITHOUT VITAMIN A FOR RESECTED, POOR-PROGNOSIS MALIGNANT MELANOMA

Meyskens, F. L., (602-882-7228) University of Arizona, Cancer Center Division, Tucson, Arizona, 85724, United States of America

PROTOCOL NUMBER(S) UARIZ-MEL-1

OBJECTIVES:

I. Determine whether Vitamin A added to BCG-Connaught increases the disease-free interval and survival of patients with melanoma.

PROTOCOL ENTRY CRITERIA: Patients with 'surgically cured' melanoma, Stage I levels 3-5 and Stage II.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Connaught, BCG, NSC-B116341.

Arm II: Immunotherapy plus Vitamin Therapy. BCG; Vitamin A, VIT-A, NSC-122759.

STRATIFICATION BY: Age: less than 30, 30-60, more than 60 years; disease stage: Stage I (levels 3, 4, and 5), Stage IIA, IIB; sex.

SPECIAL STUDY PARAMETERS: Skin tests, immunoglobulins.

END POINTS: Time to relapse; survival.

CURRENT STATUS: 55 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BCG - initially q week, maintain 2-3+ response.

Arm II: BCG - as in Arm I, plus VIT-A - 100,000 units/day po.

Therapy continued for 18 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCG - vials; Vitamin A - 50,000 unit capsules.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

9.0034 HORMONE THERAPY WITH TAMOXIFEN FOR DISSEMINATED MALIGNANT MELANOMA

Samson, M. K., (313-494-6440) Wayne State University, United Hospitals of Detroit, 4160 John R St., Detroit, Michigan, 48235, United States of America

PROTOCOL NUMBER(S) WSU-C-26878

OBJECTIVES:

I. Determine the response rate and survival of patients with disseminated melanoma treated with tamoxifen (TMX).

II. Determine the incidence of estrogen and progesterone receptors in metastatic malignant melanoma, and its correlation with response to TMX.

III. Determine the nature and extent of toxicity of TMX.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven disseminated malignant melanoma with no previous exposure to antiestrogens who are not eligible for higher priority protocols. Patients must have a minimum life expectancy of 8 weeks and adequate hematologic status.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Hormone Therapy. Tamoxifen, TMX, NSC-180973.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: SMA-17, brain and liver scans, estrogen and progesterone receptor assays.

END POINTS: Response/remission rate, objective tumor response, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 14-25 patients will be entered.

DOSAGE SCHEDULE: TMX - 20 mg po in 2 divided doses daily for at least 6 weeks. Continue therapy until disease progression or severe toxicity occurs.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: TMX - 10 mg tablets.

DATE SUMMARIZED: 11/78

9.0035 COMBINATION CHEMOTHERAPY WITH CHLOROZOTOCIN/DTIC/ACTINOMYCIN-D FOR DISSEMINATED MALIGNANT MELANOMA

Samson, M. K., (313-494-6440) Wayne State University, United Hospitals of Detroit, 4160 John R St., Detroit, Michigan, 48235, United States of America

PROTOCOL NUMBER(S) WSU-C-28178

OBJECTIVES:

I. Determine the effectiveness of the drug combination of chlorozotocin (CLZ)/DTIC/actinomycin-D (ACT-D) for remission induction, duration of remission and ultimate survival in patients with disseminated malignant melanoma.

II. Determine the nature and extent of toxicity of this three-drug combination.

PROTOCOL ENTRY CRITERIA: Patients with measurable disseminated malignant melanoma, with adequate renal and hepatic function. Patients must have a minimum life expectancy of 6 weeks and must not have had prior chemotherapy. Poor-risk patients are those over 65 years old, with wbc less than 4,000 and at least 2000, and/or prior irradiation to more than 50% of marrow bearing areas.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 3-Drug Combination Chemotherapy. Chlorozotocin, CLZ, NSC-178248; DTIC, NSC-45388; Actinomycin-D, ACT-D, NSC-3053.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: SMA-17.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment, duration of response, duration of survival.

CURRENT STATUS: At least 25 patients will be entered.

DOSAGE SCHEDULE:

Induction: CLZ - 100 mg/sqm (90 mg/sqm for poor-risk patients) iv on day 1; DTIC - 750 mg/sqm (600 mg/sqm for poor-risk patients) iv on days 1 and 21; ACT-D - 1.25 mg/sqm (1 mg/sqm for poor-risk patients) iv on days 1 and 21. Repeat course q 6 weeks. Evaluate patient at 6 weeks, unless clearly progressive disease is present after 3 weeks of therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLZ - 50 mg vials; DTIC - 100 and 200 mg ampules; ACT-D - 0.5 mg vials.

DATE SUMMARIZED: 11/78

9.0036 PHASE I-II COMBINATION CHEMOTHERAPY WITH DBD/DTIC/ACT-D FOR DISSEMINATED MALIGNANT MELANOMA

Samson, M. K., (313-494-6440) Wayne State University, Dept. of Oncology, 540 E. Canfield, Detroit, Michigan, 48201, United States of America

PROTOCOL NUMBER(S) WSU-C-38380

OBJECTIVES:

I. Determine the therapeutic efficacy of combination chemotherapy using dibromodulcitol/DTIC/actinomycin-D for remission Induction, duration of remission, and ultimate survival in patients with disseminated malignant melanoma.

II. Define the nature and extent of toxicities associated with this combination of drugs.

PROTOCOL ENTRY CRITERIA: Patients with documented disseminated malignant melanoma who have not previously received systemic chemotherapy. Patients may have received prior radiotherapy or may receive concurrent radiotherapy. The expected survival must be at least 6 weeks. Patients must have clearly measurable disease, and renal and hepatic function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Dibromodulcitol, DBD, NSC-104800; DTIC, NSC-45388; Actinomycin-D, ACT-D, NSC-3053.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Liver and kidney function tests, hematologic parameters, SMA-17, bone marrow, EKG.

END POINTS: Response/remission rate, duration of response, survival.

CURRENT STATUS: At least 25 patients will be entered.

DOSAGE SCHEDULE:

DTIC - 750 mg/sqm iv bolus on days 1 and 22; ACT-D - 1.25 mg/sqm iv bolus on days 1 and 22; DBD - 90 mg/sqm po qhs on days 3 through 7 and days 24 through 28. After treatment of 2 patients on the initial schedule, and depending on patient tolerance, DBD will be escalated in subsequent patients to 120 mg/sqm and then to 150 mg/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DBD - 50 and 100 mg tablets; DTIC - 100 and 200 mg ampules; ACT-D - 0.5 mg vials.

DATE SUMMARIZED: 12/80

9.0037 PLASMAPHERESIS IMMUNOTHERAPY OF DISSEMINATED MALIGNANT MELANOMA

Frenster, J. H., (408-279-5638) Santa Clara Valley Medical Center, 751 South Bascom Ave., San Jose, California, 95128, United States of America

PROTOCOL NUMBER(S) CA-MEL-1

OBJECTIVES:

I. Determine the response rate and duration of response to serial plasmapheresis in patients with disseminated malignant melanoma who have failed to respond to prior conventional chemotherapy and prior PHA-activated autologous lymphocyte immunotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologic documentation of disseminated malignant melanoma who have failed to respond to conventional chemotherapy and to PHA-activated autologous lymphocyte immunotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Plasmapheresis for 4 hours/day for 3 days/week for 1 week/month each month by means of the IBM Blood Cell Separator utilizing the heparin mode. Evaluation of clinical tumor parameters, peripheral blood lymphocyte parameters, and coagulation and immunoglobulin parameters each month before new course of therapy and during each course as indicated. Comparison of effects of plasmapheresis in the presence or absence of concurrent infusions of PHA-activated autologous lymphocytes. Continuation of therapeutic plasmapheresis with or without infusions of activated lymphocytes for the full duration of the response.

STRATIFICATION BY: Histologic documentation of disseminated malignant melanoma: (a) pulmonary, (b) hepatic, (c) brain, and (d) cutaneous.

SPECIAL STUDY PARAMETERS: PHA reactivity of peripheral blood lymphocytes and blood coagulation and immunoglobulin parameters before each course of plasmapheresis and during each course as indicated.

END POINTS: Objective tumor response.

CURRENT STATUS: 5 patients have been entered as of 2/80.

DOSAGE SCHEDULE:

Plasmapheresis for 4 hours/day for 3 days/ week for 1 week/month each month for the full duration of the response.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: IBM Blood Cell Separator in Heparin Plasmapheresis mode.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 00050280

9.0038 PHA-ACTIVATED AUTOLOGOUS LYMPHOCYTES FOR IMMUNOTHERAPY OF DISSEMINATED MALIGNANT MELANOMA

Frenster, J. H., (408-279-5638) Santa Clara Valley Medical Center, 751 South Bascom Ave., San Jose, California, 95128, United States of America
PROTOCOL NUMBER(S) CA-MEL-2

OBJECTIVES:

I. Determine the response rate and duration of response to the intravenous infusion of large numbers of PHA-activated autologous lymphocytes in patients with disseminated malignant melanoma who have failed prior conventional chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologic documentation of disseminated malignant melanoma unresponsive to conventional chemotherapy.

PROTOCOL OUTLINE:

Separation by means of IBM Blood Cell Separator of ten to the tenth - ten to the eleventh viable lymphocytes from peripheral blood of study patient. Separation of adherent mononuclear cells from purified lymphocytes. Incubation of purified lymphocytes with PHA or heat-inactivated PHA for 48 hours in-vitro. Separation of activated or sham-activated lymphocytes from PHA or heat-inactivated PHA. Infusion of activated or sham-activated autologous lymphocytes into study patients for 5 consecutive days each month. Evaluation of clinical tumor parameters and peripheral blood lymphocyte parameters each month before new course of therapy. Comparison of effects of infusion of activated lymphocytes with effects of infusion of sham-activated lymphocytes. Continuation of therapeutic infusions of lymphocytes in responding patients for the full duration of the response. Failing patients follow a Plasmapheresis protocol.

STRATIFICATION BY: Histologic documentation of disseminated malignant melanoma: pulmonary, hepatic, brain, cutaneous.

SPECIAL STUDY PARAMETERS: PHA reactivity of peripheral blood lymphocytes before study and monthly during course of study.

END POINTS: Tumor parameters (chest x-ray, liver function, brain CT scan): regression/stability/progression.

CURRENT STATUS: 5 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Ten to the tenth - ten to the eleventh purified activated or sham-activated autologous lymphocytes by intravenous infusion each day for 5 consecutive days each month.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Purified autologous lymphocytes either activated by PHA in-vitro or sham-activated by heat-inactivated PHA in-vitro.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 00050280

9.0039 EVALUATION OF ADJUVANT IMMUNOTHERAPY WITH TRANSFER FACTOR IN PATIENTS WITH MALIGNANT MELANOMA

Spitler, L. E., Children's Hospital of San Francisco, Laboratory of Cellular Immunology, 3700 California Street, San Francisco, California, 94118, United States of America
PROTOCOL NUMBER(S) CA-MEL-3

OBJECTIVES:

I. Study the effect of adjuvant immunotherapy with transfer factor on the disease-free interval and survival of patients with melanoma metastatic to the lung, brain, or gastrointestinal tract in whom all evident tumor has been excised and who are clinically free of tumor at the time of entry.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented Stage III melanoma with metastases to the lung, brain, or gastrointestinal tract who have undergone surgical excision of all known tumor prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy. Transfer Factor, TF, no NSC number.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Time to first recurrence, time to first visceral recurrence, survival.

CURRENT STATUS: 25 patients had been entered as of October, 1980.

DOSAGE SCHEDULE: Not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by the investigator.

DATE SUMMARIZED: 12/80

9.0040 RANDOMIZED DOUBLE-BLIND TRIAL OF TRANSFER FACTOR AS ADJUVANT THERAPY FOLLOWING RESECTION OF MALIGNANT MELANOMA

Spitler, L. E., Children's Hospital of San Francisco, Laboratory of Cellular Immunology, 3700 California Street, San Francisco, California, 94118, United States of America
PROTOCOL NUMBER(S) CA-MEL-4

OBJECTIVES:

I. Determine whether transfer factor, compared to placebo in a randomized double-blind trial, produces a lower incidence of recurrence and/or a longer disease-free interval in patients with Stage I-III malignant melanoma who have had their primary disease resected and who, in spite of a poor prognosis, are clinically free of disease at the time treatment is initiated.

II. Correlate results of immunologic tests and prognosis in these patients.

PROTOCOL ENTRY CRITERIA: Patients at least 18 years of age with histologically documented Stage I-III superficial spreading, nodular, or unclassified melanoma who are not more than 90 days post resection of primary disease and who are clinically free of disease at the time of entry. A 4-cm minimum margin of macroscopically uninvolved tissues is required, where feasible. Patients may not have lentigo maligna melanoma or primary melanoma of the eye. There may have been no prior chemotherapy, radiotherapy, or immunotherapy.

PROTOCOL OUTLINE: Randomized double-blind study.

Arm I: Immunotherapy. Transfer Factor, TF.

Arm II: Placebo Treatment.

STRATIFICATION BY: Disease Stage (I vs. II vs. III).

SPECIAL STUDY PARAMETERS: Hematologic parameters, SMA-12, chest x-ray, skin tests, DNCB sensitization and challenge, liver scan, brain scan, whole-lung tomograms, urinary melanogens.

END POINTS: Disease-free interval, interval to first visceral recurrence, survival.

CURRENT STATUS: 100 patients will be required for each arm.

DOSAGE SCHEDULE:

Arm I: TF - material from 5 x 10 to the eighth lymphocytes sc over the deltoids q 3 weeks. Continue for 2 years in the absence of recurrence. Patients will be removed from study upon the development of metastatic disease that cannot be resected.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

9.0041 ADJUVANT IMMUNOTHERAPY WITH BCG FOR STAGE III-IV MALIGNANT MELANOMA

Orr, L. E., (213-748-2411) Southern California Cancer Center, 1414 South Hope Street, Los Angeles, California, 90015, United States of America
PROTOCOL NUMBER(S) CA-SCC-275

OBJECTIVES:

I. Evaluate the efficacy of adjuvant immunotherapy in the treatment of Stages III and IV melanoma compared with historical controls.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented Stage III or IV melanoma. Stage III patients must be no more than 3 weeks post resection of primary and nodal disease. Stage IV patients may be either in clinical remission after chemotherapy or post resection of gross disease. Stage IV patients may have recurrent multiple skin metastases with no evidence of visceral involvement or they may have choroidal melanoma. Patients may not have bone, liver, bowel, or unresected brain metastases.

PROTOCOL OUTLINE: Nonrandomized study. Patients may concurrently receive Chemotherapy or Radiotherapy.

Single-agent Immunotherapy. BCG, unspecified.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Intradermal recall antigens and DNCB.

END POINTS: Immune status, tumor regression, duration of response.

CURRENT STATUS: 17 patients had been entered as of October 1980.

DOSAGE SCHEDULE:

BCG - Patients on Chemotherapy (no details given) receive biweekly BCG provided that the WBC is over 2000; patients not on Chemotherapy receive biweekly BCG; patients receiving BCG for recurrent skin metastases receive Radiotherapy (no details given) to at least one-fourth of the lesions during Immunotherapy. Follow patients responding to Immunotherapy for 3.5 years. Should disease recur or progress after more than 4 weeks of Immunotherapy, remove patient from study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

9.0042 RANDOMIZED PHASE III EVALUATION OF BCG PLUS DTIC AS ADJUVANT THERAPY IN PATIENTS WITH STAGES I-II MALIGNANT MELANOMA

Cosimi, A. B., (617-726-8256) Massachusetts General Hospital, Department of Surgery, Boston, Massachusetts, 02114, United States of America
PROTOCOL NUMBER(S) MA-MEL-1; MA-MSH-10/4

OBJECTIVES:

I. Determine the therapeutic efficacy of adjuvant chemoimmunotherapy using DTIC and BCG in patients with Stages I and II malignant melanoma in a randomized Phase III study.

II. Establish the effect of adjuvant therapy on the patterns of recurrence of malignant melanoma.

III. Evaluate the feasibility of tine puncture BCG immunotherapy in a large, multi-institution group.

PROTOCOL ENTRY CRITERIA: Patients between the ages of 18 and 80 years with histologically documented Stage Ib or II primary cutaneous melanoma who have no distant metastases and who are within 60 days of adequate surgical resection. Patients with recurrent or later appearance of metastases must have had resection of all clinically evident tumor and be without evidence of distant metastases. A second group to be entered and separately stratified include those with recurrent melanoma that is totally resectable. Patients must be in good general health and not have any other uncontrolled malignancy.

PROTOCOL OUTLINE: Randomized study. Patients are randomized to receive chemoimmunotherapy or no adjuvant therapy.

Arm I: Single-agent Chemotherapy plus Immunotherapy. DTIC, NSC-45388; plus BCG-Tice, BCG, NSC-B116327.

Arm II: No treatment.

STRATIFICATION BY: Stage of disease (Ib vs. II), prior lymph node dissection in Stage Ib patients (yes vs. no), lymph node status in Stage II patients (clinically negative vs. palpably enlarged), site of recurrence for patients with recurrent disease (local or regional failure vs. distant metastases).

SPECIAL STUDY PARAMETERS: Hematological parameters, liver and kidney function tests, chest x-ray.

END POINTS: Rate of recurrence, survival.

CURRENT STATUS: 60-75 patients will be accrued annually.

DOSAGE SCHEDULE:

Arm I: DTIC - 200 mg/sqm/day iv over 20-30 minutes for 4 days at monthly intervals for 6 months, then q 2 months for 6 months, then q 3 months for the second year; BCG - 1 ampule by tine scarification q 2 weeks for 12 weeks, then q 4 weeks for a total of 2 years, with the first treatment given 1 week prior to initiating DTIC therapy.

Arm II: No treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DTIC - 200 mg ampules.

DATE SUMMARIZED: 12/80

9.0043 IMMUNOTHERAPY WITH BCG VS BCG PLUS CHEMOTHERAPY WITH DTIC FOR DISSEMINATED MELANOMA

Kerry, R. L., (313-973-2800) St. Joseph's Mercy Hospital, P.O. Box 995, Ann Arbor, Michigan, 48106, United States of America
PROTOCOL NUMBER(S) MI-MEL-1

OBJECTIVES:

I. Compare the remission rates, survival times and cure rates in patients who have disseminated melanoma treated by immunotherapy with BCG-Tice (BCG) plus chemotherapy with dacarbazine (DTIC), by BCG immunotherapy alone, or (controls) by neither of these modalities.

PROTOCOL ENTRY CRITERIA: Any patient with disseminated melanoma.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-116327.

Arm II: Single-agent Chemotherapy plus Immunotherapy. Dacarbazine, DTIC, NSC-45388; plus BCG.

Arm III: No further treatment.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BCG by multipuncture tine technique started before or after biopsy, or 2-4 weeks after operation. Administration in both axillae and groin areas; a fifth site may be added depending on tumor location. BCG given weekly for 12 weeks, then every other week for 2 years.

Arm II: BCG as in Arm I; DTIC (dosage and schedule not given).

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 2-8 x 10 to the eighth colony-forming units/ampule; DTIC - not given.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

9.0044 IMMUNOTHERAPY WITH BCG IN ADJUVANT TREATMENT BEFORE AND AFTER SURGERY FOR MELANOMA, STAGES I AND II

Kerry, R. L., (313-973-2800) St. Joseph's Mercy Hospital, P.O. Box 995, Ann Arbor, Michigan, 48106, United States of America
PROTOCOL NUMBER(S) MI-MEL-2

OBJECTIVES:

I. Determine whether adjuvant immunotherapy with BCG-Tice will improve the cure rate of melanoma when added to potentially curative surgery.

PROTOCOL ENTRY CRITERIA: All patients with melanoma who will have the primary tumor site excised, with at least a five-cm margin in all locations except the face, along with simultaneous regional lymphadenectomy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy plus Surgery. BCG-Tice, BCG, NSC-B116327; plus biopsy plus excision of primary and regional nodes.

Arm II: Surgery plus Immunotherapy. BCG-Tice; plus biopsy plus excision of primary and regional nodes.

Arm III: Surgery plus Immunotherapy. Biopsy plus excision of primary and regional nodes; plus BCG.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be admitted.

DOSAGE SCHEDULE:

Arm I: BCG - by multipuncture tine technique in both axillae and groin areas to be started before biopsy and surgery, and given weekly for 12 weeks, then every other week for 2 years.

Arm II: Biopsy followed by BCG as in Arm I and preceding surgery.

Arm III: Biopsy and surgery followed within 2-4 weeks by BCG as in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - ampules containing 2-8 x 10 to the eighth colony-forming units.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

9.0045 RANDOMIZED ADJUVANT STUDY OF VACCINIA ONCOLYSATE VS BCG IN STAGE I MALIGNANT MELANOMA

Wallack, M. K., (314-454-2919) Washington University School of Medicine, Department of Surgery, 4960 Audubon Avenue, St. Louis, Missouri, 63110, United States of America
PROTOCOL NUMBER(S) MO-MEL-2

OBJECTIVES:

I. Measure the effect of vaccinia oncolysate vs. BCG on the disease-free interval of patients with Stage I melanoma at high risk.

II. Observe effect of vaccinia oncolysate and BCG on survival of these patients.

PROTOCOL ENTRY CRITERIA: Patients with Stage I melanoma (T1, T2, N0, M0) of the extremities with primary tumor surgically removed with an adequate surgical margin. Lymph node dissection required if depth of invasion is equal to or greater than 1.5 mm. Nodes must be free of tumor.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. Vaccinia oncolysate.

Arm II: Immunotherapy. BCG-Glaxo, BCG.

STRATIFICATION BY: Node dissection: yes vs. no; sex; Clarks level; depth of invasion.

SPECIAL STUDY PARAMETERS: Skin tests; antibody titers; liver, brain, and bone scans; upper G.I. with small bowel follow-through; CXR.

END POINTS: Disease-free interval, survival.

CURRENT STATUS: 2 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: Vaccinia oncolysate - 2 cc id in four divided doses in week one, then 1 cc weekly for 12 weeks, then every other week for 24 months.

Arm II: BCG - 1 cc vial by tine technique in each extremity weekly for 13 weeks, then every other week for 24 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Vaccinia oncolysate - 1 cc vials; BCG - 1 cc vials.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

9.0046 PHASE II IMMUNOTHERAPY WITH VACCINIA ONCOLYSATE VS CHEMOTHERAPY WITH CTX AND DTIC FOR STAGES I AND II MELANOMA

Wallack, M. K., (314-454-2919) Washington University School of Medicine, Department of Surgery, 4960 Audubon Avenue, St. Louis, Missouri, 63110, United States of America
PROTOCOL NUMBER(S) MO-MEL-3

OBJECTIVES:

I. Compare the effectiveness of vaccinia oncolyste vs. dacarbazine (DTIC) and Cytoxan (cyclophosphamide, CTX) on the disease-free interval in melanoma (histological Stage II disease of the extremity and histological Stage I disease of the head, neck, trunk, and genitalia).

II. Compare the effect of these agents on survival in the same patient population.

PROTOCOL ENTRY CRITERIA: Patients with extremity lesions with 1-3 positive nodes and patients with head, neck, trunk, and genitalia lesions with greater than 1.5 mm depth of invasion with histologically negative nodes.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Immunotherapy. Vaccinia oncolysate.

Arm II: 2-Drug Combination Chemotherapy. Cytoxan (Cyclophosphamide), CTX, NSC-26271; Dacarbazine, DTIC, NSC-45388.

STRATIFICATION BY: Sex, pathological stage, number of positive nodes, location and depth of invasion.

SPECIAL STUDY PARAMETERS: Skin tests; antibody titers; liver, brain, and bone scans; UGI with small bowel follow-through; CXR.

END POINTS: Disease-free interval, survival.

CURRENT STATUS: 3 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: Vaccinia oncolysate - 2 ampules in 4 divided doses in week 1, then 1 ampule for 12 weeks, then every other week for 24 months.

Arm II: DTIC - 600 mg/sqm iv; CTX - 600 mg/sqm iv every 3 weeks for 12 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Vaccinia oncolysate - 1 ml ampules; DTIC - 100 and 200 mg vials; CTX - 100, 200, and 500 mg vials.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

9.0047 PHASE II CHEMOTHERAPY WITH DTIC/CTX PLUS IMMUNOTHERAPY WITH VACCINIA ONCOLYSATE FOR ADVANCED STAGE I OR STAGE II MELANOMA

Wallack, M. K., (314-454-2919) Washington University School of Medicine, Department of Surgery, 4960 Audubon Avenue, St. Louis, Missouri, 63110, United States of America
PROTOCOL NUMBER(S) MO-MEL-4

OBJECTIVES:

I. Determine the effectiveness of DTIC, Cytoxan, and vaccinia oncolysate in improving the disease-free interval of melanoma patients following surgical removal of all existing disease in clinical Stage I patients with four or more positive microscopic nodes or clinical Stage II disease with a positive macroscopic node.

II. Observe survival time in these patients.

PROTOCOL ENTRY CRITERIA: Clinical Stage I melanoma patients with 4 or more positive microscopic nodes or patients with Stage II disease with palpable nodes and with no previous chemo- or immunotherapy.

PROTOCOL OUTLINE: Nonrandomized study. Therapy begins within 6-8 weeks of surgery.

Immunotherapy plus 2-Drug Combination Chemotherapy. Vaccinia oncolysate plus Dacarbazine, DTIC, NSC-45388; Cytoxan (Cyclophosphamide), CTX, NSC-26271.

STRATIFICATION BY: Sex, current pathological stage, prior pathological stage, location of primary melanoma.

SPECIAL STUDY PARAMETERS: Antibody titers; liver, brain, and bone scans; CXR; UGI; skin tests.

END POINTS: Disease-free interval, survival.

CURRENT STATUS: 5 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Vaccinia oncolysate - 2 ampules id, 4 divided doses in week 1, then 1 ml q week for 12 weeks, then alternate weeks for 24 months. DTIC - 600 mg/sqm iv; CTX - 600 mg/sqm iv every 3 weeks for total of 9 courses. DTIC and CTX start on week 3.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Vaccinia oncolysate - 1 ml ampules; DTIC - 100 and 200 mg vials; CTX - 100, 200, and 500 mg vials.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

9.0048 SPECIFIC ACTIVE IMMUNOTHERAPY WITH IRRADIATED NEURAMIDASE-TREATED MELANOMA CELLS PLUS BCG (ADJUVANT) FOR MELANOMA

Seigler, H. F., Duke Medical Center, P.O. Box 3917, Durham, North Carolina, 27710, United States of America
PROTOCOL NUMBER(S) NC-MEL-1

OBJECTIVES:

I. Determine the effectiveness of specific active immunotherapy with BCG adjuvant in patients with Stage I or II melanoma.

PROTOCOL ENTRY CRITERIA: Patients with Stage I or II melanoma, Clark's level III, IV, or V primaries, free of disease involving viscera or bone and of multiple lesions of the CNS.

PROTOCOL OUTLINE: Nonrandomized study.

Two-agent Immunotherapy. X-irradiated neuraminidase-treated melanoma cells; plus BCG-Glaxo, no NSC number.

STRATIFICATION BY: Known nodal metastases: yes vs. no; local recurrence: yes vs. no.

SPECIAL STUDY PARAMETERS: Post-immunization serum samples are monitored for tumor specific antibody utilizing complement dependent cytolysis.

END POINTS: None given.

CURRENT STATUS: 1500 patients will be entered.

DOSAGE SCHEDULE:

Patients are sequentially immunized - 2.5 x 10 to the seventh x-irradiated neuraminidase-treated melanoma cells, and BCG is admixed sc for its adjuvant effect. Patients with Clark's Level III, IV, or V primaries without known metastasis are immunized until tumor specific antibody is evident in the patient's sera. Immunization schedule is then stopped and the patients are monitored in the clinic. Patients with Clark's Level III, IV, or V primaries and either local recurrence or nodal metastases are serially immunized until tumor antibody is evident in the serum. Patients are then hyperimmunized with three subsequent boosters to increase the melanoma antibody titer and monitored on a quarterly basis in the clinic.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

9.0049 CHEMOTHERAPY WITH DTIC VS DTIC PLUS ADJUVANT IMMUNOTHERAPY WITH C. PARVUM IN HIGH-RISK MELANOMA

Murray, J. L., (405-235-8331, Ext. 442) Oklahoma Medical Research Foundation, 825 N.E. 13th St., Oklahoma City, Oklahoma, 73104, United States of America
PROTOCOL NUMBER(S) OK-MEL-1; OMRF-7905; OMRF-7403

OBJECTIVES:

I. Determine the effect of adjuvant immunotherapy with DTIC and C. parvum in prolonging disease-free interval and survival.

PROTOCOL ENTRY CRITERIA: Patients with primary malignant melanoma who have undergone wide resection with or without regional node dissection or patients with solitary metastatic disease that has been completely resected, Clark's Level III-IV lesions (less than 1.5 mm thickness), Clark's Level V lesions (greater than 1.5 mm thickness), and those with local or regional recurrent disease, regional lymph node involvement, and resected distant metastases.

PROTOCOL OUTLINE: Randomized study. Group I patients (Clark's Level III-IV lesions, less than 1.5 mm thickness) are randomized to Arms I and II; Group II patients (Clark's Level V lesions, greater than 1.5 mm thickness, and those with local or regional recurrent disease, regional lymph node involvement, and resected distant metastases) are randomized to Arms III and IV.

Arm I: Immunotherapy. Corynebacterium parvum, Burroughs-Wellcome, C. parvum, B.W., NSC-220537.

Arm II: No treatment.

Arm III: Single-agent Chemotherapy. DTIC, NSC-45388.

Arm IV: Chemotherapy plus Immunotherapy. DTIC plus C. parvum, B.W.

STRATIFICATION BY: Prognosis: good vs. poor.

SPECIAL STUDY PARAMETERS: Weekly CBC, liver and renal function tests q 2-3 months, chest x-rays q 4-6 months, immunologic testing q 4-6 months including serum testing for tumor antigen.

END POINTS: Recurrence and survival; toxicity.

CURRENT STATUS: 60 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Enter patients within one month of surgery.

Arm I: C. parvum, B.W. - 4 mg (0.5 cc) sc weekly for 6 weeks, thereafter monthly for 6 months. Continue treatment until relapse or for up to 5 years.

Arm II: No treatment.

Arm III: DTIC - 850 mg/sqm iv monthly for 6 months.

Arm IV: DTIC - 850 mg/sqm iv monthly for 6 months; plus C. parvum, B.W. - 4 mg sc weekly on days 7, 14, and 21 during DTIC, then q 2 weeks for 6 months and thereafter monthly for up to 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DTIC - 100 and 200 mg ampules; C. parvum - 1.2 ml vials.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 00600280

9.0050 MER AS ADJUVANT THERAPY IN CHOROIDAL MELANOMA

Berd, D., (215-728-2656) Fox Chase Cancer Center, 7701 Burholme Ave., Philadelphia, Pennsylvania, 19111, United States of America
PROTOCOL NUMBER(S) PA-MEL-1

OBJECTIVES:

I. Determine whether therapy with MER-BCG prolongs the disease-free interval and/or survival of patients who have undergone enucleation for high-risk choroidal melanoma.

PROTOCOL ENTRY CRITERIA: Patients who have undergone enucleation for choroidal melanoma of mixed cell, epithelial, or necrotic type.

PROTOCOL OUTLINE: Randomized study.

Arm I: No treatment.

Arm II: Immunotherapy. MER-BCG, MER, NSC-143769.

STRATIFICATION BY: Age, cell type, greatest diameter, frequency of mitotic figures, extent of scleral invasion.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Development of metastases and death.

CURRENT STATUS: 70 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

MER - dose required to produce moderate local reaction (0.1-1.0 mg): week 1 - 1.0 mg id; week 2 - 0.5 mg id; week 3 - 0.25 mg id; week 4 - 0.10 mg id; then monthly for 11 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: MER in vials of 1.0 mg/ml.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

PATIENT ACCRUAL: 00700280

9.0051 ADJUVANT IMMUNOTHERAPY WITH C. PARVUM VS BCG FOR STAGE I AND II MALIGNANT MELANOMA

Harvey, H. A., (717-534-8677) Milton S. Hershey Medical Center, The Pennsylvania State University, Hershey, Pennsylvania, 17033, United States of America

PROTOCOL NUMBER(S) PA-MSHMC-MEL-2

OBJECTIVES:

I. Assess the effectiveness of immunotherapy with C. parvum vs. BCG in patients with Stage I and II melanoma who are at risk of developing recurrent disease.

PROTOCOL ENTRY CRITERIA: Patients between 21 and 75 years of age with Stage I (Clark's levels 3 to 5) or Stage II melanoma.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: Immunotherapy. Corynebacterium parvum, Burroughs-Wellcome, C. parvum, B.W., NSC-220537.

STRATIFICATION BY: Disease stage, tumor site (trunk vs. extremity vs. head and neck).

SPECIAL STUDY PARAMETERS: CBC and Panel D; chest x-ray, quantitative immunoglobulins; skin tests: PPD, Mumps, Candida, Tetanus, SK/SD, DNCB.

END POINTS: Recurrence rate, length of survival.

CURRENT STATUS: 114 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: BCG - 3 x 10 to the eighth organisms id by 36-prong technique weekly q 4 weeks, then q other week for 4 treatments and monthly for 6 months. Treatment is then q 2 months for up to 2 years. The median duration of followup is 18 months.

Arm II: C. parvum, B.W. - 5 mg/sqm sc on same schedule as for BCG in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

9.0052 SURGERY FOR STAGE I AND CHEMOTHERAPY WITH ACT-D/VCR/CTX FOR STAGE II-III MELANOMA IN CHILDREN

Hayes, F. A., (901-522-0500) St. Jude Childrens Research Hospital, 332 N. Lauderdale St., P.O. Box 318, Memphis, Tennessee, 38101, United States of America

PROTOCOL NUMBER(S) SJCRH-MELANO

OBJECTIVES:

I. Evaluate combination chemotherapy using actinomycin-D, cyclophosphamide, and vincristine for Induction in children with Stage II-III melanoma.

II. Treat Stage I children with melanoma surgically.

PROTOCOL ENTRY CRITERIA: Patients under the age of 25 years with a diagnosis of malignant melanoma.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with Stage I disease to Regimen A and those with Stage II-III disease to Regimen B.

Regimen A: Surgery.

Regimen B: 3-Drug Combination Chemotherapy. Actinomycin-D, ACT-D, NSC-3053; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Stage (I vs. II and III).

SPECIAL STUDY PARAMETERS: CT scans, bone scan, liver scan, appropriate radiographs.

END POINTS: Response/remission rate, duration of remission.

CURRENT STATUS: 7 patients were entered as of September 1980.

DOSAGE SCHEDULE: Not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by the investigator.

DATE SUMMARIZED: 12/80

9.0053 ADJUVANT CHEMO-IMMUNOTHERAPY WITH DTIC PLUS BCG VS MECCNU PLUS BCG FOR STAGES I AND II MALIGNANT MELANOMA

Oldham, R. K., (615-322-4967) Vanderbilt University, Division of Oncology, Department of Medicine, Nashville, Tennessee, 37232, United States of America

PROTOCOL NUMBER(S) TN-MEL-M1

OBJECTIVES:

I. Determine whether one of two forms of chemo-immunotherapy, dacarbazine (DTIC) plus BCG-Pasteur vs. methyl-CCNU (MeCCNU) plus BCG-Pasteur, is more effective and determine the effect of chemo-immunotherapy on the immune response of patients with malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with resected Stage I (level 3 or greater) or resected Stage II malignant melanoma.

PROTOCOL OUTLINE: Randomized study. Patients are randomized following resection of the primary tumor and the regional nodes.

Arm I: Single-agent Chemotherapy plus Immunotherapy. Dacarbazine, DTIC, NSC-45388; BCG-Pasteur, BCG, NSC-B116328.

Arm II: Single-agent Chemotherapy plus Immunotherapy. Methyl-CCNU, MeCCNU, NSC-95441; BCG-Pasteur, BCG, NSC-B116328.

STRATIFICATION BY: Sex, tumor site, and disease stage.

SPECIAL STUDY PARAMETERS: Immunological evaluation.

END POINTS: Recurrence and survival.

CURRENT STATUS: 45 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: DTIC - 200 mg/sqm iv q 5 days for 28 days; BCG - 1 ampule by Heaf gun scarification on days 1 and 15. DTIC given for 6 cycles, then BCG for 6 cycles; cycle length, 28 days.

Arm II: MeCCNU - 150 mg/sqm po on day 1; BCG - 1 ampule by Heaf gun scarification on days 1 and 15. MeCCNU given for 6 cycles, then BCG for 6 cycles; cycle length, 36 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/80

9.0054 IMMUNOCHEMOTHERAPY WITH BCG PLUS DTIC VS DEPIGMENTATION THERAPY WITH MBEH FOR RESECTED MELANOMA

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PROTOCOL NUMBER(S) YALE-3479; HIC-1869

OBJECTIVES:

I. Evaluate the efficacy of DTIC and BCG, as well as MBEH (monobenzyl ether of hydroquinone), in the adjuvant treatment of patients with cutaneous malignant melanoma.

II. Evaluate the role of nonspecific immunotherapy and depigmentation therapy with these agents in specific antitumor responses measured by autologous assays.

PROTOCOL ENTRY CRITERIA: Patients with greater than 0.76 mm deep, Clark level III, IV or V melanoma with no evidence of lymph node invasion (Stage I) or with pathologically positive lymph nodes at time of surgery (Stage II). Patients must have undergone resection of all clinically evident tumor within 90 days prior to entry. There must be no evidence of distant dissemination or visceral involvement. Patients must have a normal hematologic profile and normal renal and hepatic function. There must be no active tuberculosis; women patients must not be pregnant. Patients must not be on concurrent therapy with estrogens or other antineoplastic agents.

PROTOCOL OUTLINE: Randomized study. Failures on Arm I or II may cross over to the other arm.

Arm I: Single-agent Chemotherapy plus Single-agent Immunotherapy. DTIC, NSC-45388; plus BCG-Tice, BCG, NSC-B116327.

Arm II: Depigmentation Therapy. MBEH (monobenzyl ether of hydroquinone).

Arm III: Intensive observation.

STRATIFICATION BY: Stage and primary thickness: Stage I, 0.76-1.50 mm vs. Stage I, 1.55-3.99 mm vs. Stage I, 4.0 mm and greater vs. all Stage II; sex; age: 0 to 30 years vs. 30 to 60 years vs. greater than 60 years; disease site: trunk vs. extremity; surgical/pathologic evaluation of nodes (lymphadenectomy vs. no lymphadenectomy for definition of Stage II).

SPECIAL STUDY PARAMETERS: Serology and cell-mediated cytotoxicity, tomographic gallium scanning, liver and spleen scans, chest x-ray, skin tests.

END POINTS: Disease-free interval.

CURRENT STATUS: The probable duration of the project is 4-5 years.

DOSAGE SCHEDULE:

Arm I: BCG - 5 x 10 to the 8th viable cells id q 2 weeks for 3 months, then q 4 weeks for a total of 2 years; DTIC - 200 mg/sqm/day for 3 days or 600 mg/sqm/day iv over 20 to 30 minutes q month for 6 months, then q other month for 6 months, then every 3 months for one year. DTIC therapy is initiated one week after the start of BCG therapy. Therapy is discontinued when unacceptable toxicity develops or there is disease recurrence.

Arm II: MBEH - the 20 percent ointment is administered topically over the skin of the anterior thigh over an area 5 x 10 cm on each leg, twice daily. The frequency may be increased to 3 or 4 times daily. In the absence of toxicity, therapy will continue for 2 years.

Arm III: Observation only. At disease recurrence, patients may be randomized to Arms I and II.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: DTIC - 200 mg ampules; MBEH - 20 percent ointment.

DATE SUMMARIZED: 01/81

9.0055 PHASE II IMMUNOTHERAPY WITH HUMAN LEUKOCYTE INTERFERON FOR METASTATIC MELANOMA

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PROTOCOL NUMBER(S) YALE-3519; HIC-1832

OBJECTIVES:

I. Determine the efficacy of interferon against metastatic melanoma.

II. Determine whether interferon has any detrimental effects on nitrogen balance, the functioning of the pituitary endocrine axis or the immune reactivity of the patient against the melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic melanoma, with documented multiple metastases of skin, subcutaneous tissue, or the lymph nodes. Metastases should be easily measured. There must be no visceral metastases other than lung. Patients must be over 18 years of age and have a life expectancy greater than 6 months. Karnofsky performance status must be greater than 50 percent, and there must be adequate bone marrow reserve and hematologic function. Patients must receive no treatment for metastases for 30 days prior to entry.

PROTOCOL OUTLINE: Patients are randomly assigned to one of three dose levels.

Single-agent Immunotherapy. Human Leukocyte Interferon, IF.

STRATIFICATION BY: Extent of disease: lymph node and soft tissue disease, without lung metastases vs. lung involvement, with or without lymph nodes/soft tissue involvement.

SPECIAL STUDY PARAMETERS: Complex metabolic profile to include pituitary axis and organ studies, nitrogen balance studies, non-specific and tumor-specific cellular and serological immune studies, tumor measurements.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Twenty-four patients will be entered; the probable duration of the project is 2 years.

DOSAGE SCHEDULE:

IF - 1, 3, or 9 million units subcutaneously in 2 equally divided doses at 6 AM and 6 PM daily for 6 weeks (42 days). Treatment is withdrawn when disease progression is noted.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: IF - 5 x 10 to the 5th IU, 1 x 10 to the 6th IU, 1.5 x 10 to the 6th IU, 5 x 10 to the 6th IU, (one dose/syringe).

DATE SUMMARIZED: 10/80

9.0056 PHASE I-II IMMUNOTHERAPY WITH IMMUNE INTERFERON FOR METASTATIC MELANOMA

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PROTOCOL NUMBER(S) YALE-3580; HIC-2114

OBJECTIVES:

I. Evaluate immune interferon at escalating dosages (Phase I-II) in patients with melanoma.

PROTOCOL ENTRY CRITERIA: Patients between the ages of 19 and 74 with measurable, histologically proven, metastatic or recurrent melanoma with no extrapulmonary acutely life-threatening visceral metastasis. Patients must have an estimated life expectancy greater than 3 months and a performance status of 0 or 1 on the ECOG scale. Patients must have adequate hematological parameters and normal liver and renal function. The delayed hypersensitivity to PPD intermediate intradermal skin test (5 tuberculin units) must be greater than 20 mm at 48 hours.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Immunotherapy. Immune Interferon, ImIF.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic function tests; liver and renal function tests; immunological assessment: T and B cell quantitation, immunoglobulin, natural killer cell assay, macrophage phagocytosis assay, cellular immune cytotoxicity, serology assay against cultured autologous melanoma cells, skin tests, delayed hypersensitivity response to PPD and DNCB.

END POINTS: Response/remission rate, objective tumor response, toxicity of treatment, pharmacokinesis of immune interferon.

CURRENT STATUS: 10-15 patients will enter the Phase I trial.

DOSAGE SCHEDULE:

Phase I: ImIF - 1 x 10 to the 3rd units im daily for 4 days, escalating dosage to 5 x 10 to the 3rd, 2.5 x 10 to the 4th, 1.25 x 10 to the 5th, 6.25 x 10 to the 5th, and 3 x 10 to the 6th units/day. If no toxicity is seen at 3 x 10 to the 6th units im daily, change to iv route beginning with 1 x 10 to the 3rd units and escalating dosage as in the im trial. Duration of treatment will be determined by maximum tolerated dose of ImIF in the patient.

Phase II: Dosage of ImIF based on the limiting toxicity observed in the Phase I trial will be employed for Phase II trials. If neither im or iv trials are associated with toxicity, an arbitrary dosage of 1-6 x 10 to the 5th units im will be employed. This will allow for 2-3 weeks of therapy in the outpatient department following 7-10 days of initial observations while hospitalized.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/80

9.0057 ADJUVANT IMMUNOTHERAPY WITH MER-BCG FOR HIGH-RISK MALIGNANT MELANOMA OF THE HEAD, NECK, AND EXTREMITIES

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PROTOCOL NUMBER(S) YALE-3877; HIC-1351

OBJECTIVES:

I. Determine whether adjuvant immunotherapy with MER-BCG used in high-risk patients will prolong the disease-free interval or survival rate in malignant melanoma.

II. Determine whether direct immunologic stimulation of regional draining nodes is a more efficacious route of immunotherapy.

III. Determine histologic alterations of regional draining nodes by intralymphatic immunization in melanoma of extremities.

IV. Determine whether the results of a prospective testing of specific immunocompetence can predict which patients are in a high-risk category for recurrence.

PROTOCOL ENTRY CRITERIA: Patients with melanoma who have undergone incisional or excisional biopsy to confirm the diagnosis of melanoma and to determine the depth of invasion. Disease must be Stage I, Clark level IV or V, Breslow depth greater than 1.5 mm or Stage II. Patients with evidence of spread of disease beyond the regional draining nodes are excluded.

PROTOCOL OUTLINE: Patients with head and neck disease enter Regimen A; patients with disease located on the extremities enter Regimen B. All patients are concurrently randomized to Arms I, II, III, and IV.

Regimen A: Surgery. Local excision and radical neck dissection.

Regimen B: Surgery plus Single-agent Chemotherapy. Excision of tumor plus regional lymphadenectomy plus DTIC, NSC-45388. One-half of the patients entered on this regimen receive preoperative Immunotherapy with MER-BCG, MER, NSC-143769.

Arm I: Single-agent Immunotherapy. MER, on a monthly postoperative schedule.

Arm II: Single-agent Immunotherapy. MER, intraoperative instillation.

Arm III: Single-agent Immunotherapy. MER, intraoperative instillation, plus monthly postoperative immunizations.

Arm IV: No further treatment.

STRATIFICATION BY: Site of disease: head and neck vs. extremities.

SPECIAL STUDY PARAMETERS: Immunologic competence status tests, lymphangiogram.

END POINTS: Disease-free interval, survival rate, time to relapse.

CURRENT STATUS: 19 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Regimen A: Local excision and radical neck dissection.

Regimen B: Excision of tumor plus regional lymphadenectomy plus DTIC - 850 mg/sqm perfused by a pump oxygenator via both an arterial and a venous line in the major vessels to the extremity for 1 hour, at a slow rate of 100-400 cc per minute. Following the perfusion, the drug is flushed by additional infusion of 2 liters of lactated Ringer's solution, and 2 units of dextran. Half of the patients on this regimen receive preoperative MER - 0.2 mg infused via catheter into the lymphatic channel.

Arm I: Beginning 6 weeks postoperatively, MER - 1 mg id by tine multiprong technique at 5 sites (0.2 mg per site) q month for 6 months.

Arm II: MER - 0.2 mg injected into the soft tissues in various sites within the area of the regional draining nodes after the lymphadenectomy.

Arm III: MER as in Arm I plus MER as in Arm II.

Arm IV: No further treatment.

All patients with a positive reaction to intermediate strength PPD will be considered for a 50 percent reduction in the MER dose.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

9.0058 PHASE II DTIC/VCR/MER-BCG VS DTIC/VCR/C.PARVUM INDUCTION AND VCR/MTX/MER-BCG VS VCR/MTX/C.PARVUM MAINTENANCE FOR STAGE V MELANOMA

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PROTOCOL NUMBER(S) ARG-OSITC-3003

OBJECTIVES:

I. Determine whether MER-BCG vs. C. parvum immunotherapy during chemotherapy induction with DTIC/VCR is ineffective, decreases, or increases the percentage of remissions and survivals in patients with advanced melanomas.

II. Establish whether MER-BCG or C. parvum changes the patient's initial immunologic parameters.

III. Evaluate the beneficial effects of MER-BCG and C. parvum as determined by morbidity and toxicity during various phases.

IV. Maintain remission with continuous immunotherapy with MER-BCG or C. parvum.

PROTOCOL ENTRY CRITERIA: Patients less than 75 years old with histologically confirmed and objectively evaluable lesions of Clarks grade V advanced melanoma with distant metastases. Patients must have a minimum life expectancy of 3 months, a Karnofsky performance status of 50 or more, adequate hematologic, renal, and hepatic function, and have received no prior Chemotherapy or Immunotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I:

Induction:

2-Drug Combination Chemotherapy plus Immunotherapy. Vincristine, VCR, NSC-67574; DTIC, NSC-45388; MER-BCG, MER, NSC-143769.

Maintenance:

2-Drug Combination Chemotherapy plus Immunotherapy. VCR; Methotrexate, MTX, NSC-740; plus MER.

Arm II:

Induction:

2-Drug Combination Chemotherapy plus Immunotherapy. VCR; DTIC, plus C. parvum, NSC-197213.

Maintenance:

2-Drug Combination Chemotherapy plus Immunotherapy. VCR; MTX; plus C. parvum.

STRATIFICATION BY: Age, metastatic sites, hepatic involvement, participating institutions.

SPECIAL STUDY PARAMETERS: Skin tests; lymphocyte reactions: blast transformation, rosette test; immunoglobulin levels; complement determination; echocardiogram; liver, brain, and bone scans.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 40 patients will be entered.

DOSAGE SCHEDULE:

Arm I:

Induction:

VCR - 1.4 mg/sqm iv on day 1; DTIC - 140 mg/sqm iv 6 hours after VCR on days 1 through 5; MER - 200 micrograms in 5 different sites for a total daily dose of 1 mg on days 1 and 15. Repeat course q 28 days for 8 courses.

Maintenance:

VCR - as in Induction; MTX - 30 mg/sqm iv 6 hours following VCR on day 1; MER - as in Induction on day 8. Repeat course q 21 days for 8 courses, or until remission or intolerance.

Arm II:

Induction:

VCR and DTIC - as in Arm I; C. parvum - 0.35 mg/sqm iv on day 1, 0.75 mg/sqm on day 3, 1.0 mg/sqm on day 5, 2.5 mg/sqm on days 8 and 15 of first course and continue with this dosage on days 1 and 14 of remaining courses. Repeat course q 28 days for 8 courses.

Maintenance:

VCR and MTX - as in Arm I; C. parvum - 2.5 mg/sqm iv on days 1 and 15. Repeat course q 21 days for 8 courses or until remission or intolerance.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DTIC - 100 and 200 mg vials; VCR - 1 mg vials; MTX -5 and 50 mg vials; MER - 1 mg ampules; C. parvum - 4 mg ampules.

DATE SUMMARIZED: 05/79

9.0059 COMBINATION CHEMOTHERAPY WITH CCNU/DTIC PLUS IMMUNOTHERAPY WITH BCG FOR STAGE II AND III MELANOMA

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PROTOCOL NUMBER(S) CAN-MEL-1

OBJECTIVES:

I. Compare the efficacy of chemo/immunotherapy with BCG by tine scarification plus DTIC vs. BCG plus CCNU vs. BCG plus DTIC plus CCNU.

PROTOCOL ENTRY CRITERIA: Patients with cutaneous melanoma Stage II and III.

PROTOCOL OUTLINE: Randomized study. All patients will undergo wide local excision of tumor with or without skin graft and regional node dissection prior to randomization.

Arm I: Single-agent Chemotherapy plus Immunotherapy. DTIC, NSC-45388; plus BCG-Pasteur, BCG, NSC-B116328.

Arm II: Single-agent Chemotherapy plus Immunotherapy. CCNU, NSC-79037; plus BCG.

Arm III: Two-Drug Combination Chemotherapy plus Immunotherapy. DTIC; CCNU; plus BCG.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: SMAC, complete hemogram, bone and liver scan, chest x-ray.

END POINTS: Duration of response, recurrence rate, disease-free interval.

CURRENT STATUS: 88 patients have been entered as of October 1980.

DOSAGE SCHEDULE:

Arm I: BCG; DTIC (no dosages or schedule given).

Arm II: CCNU; BCG (no dosages or schedule given).

Arm III; DTIC; CCNU; BCG (no dosages or schedule given).

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 12/80

9.0060 ADJUVANT IMMUNOTHERAPY WITH BCG OR LEVAMISOLE OR BOTH FOR MALIGNANT MELANOMA

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PROTOCOL NUMBER(S) CAN-NCIC-ME1

OBJECTIVES:

I. Test three forms of immunotherapy, BCG-Connaught (BCG), levamisole (LEV), and BCG/LEV as an adjuvant treatment against a no treatment control in patients with completely resected malignant melanoma.

II. Compare the Clark classification with the method of measuring the depth of the lesion in millimeters as an index of prognosis.

III. Set up a country-wide registry of this disease so as to accumulate epidemiological data on malignant melanoma in Canada.

PROTOCOL ENTRY CRITERIA: Patients between 17 and 70 years old with histologically confirmed Stage I, II or III superficial spreading melanoma or nodular melanoma. Patients must enter within 12 weeks of definitive surgery which removed all known disease. Patients must have a minimum life expectancy of over 3 months, no prior therapy for this disease, no concurrent active tuberculosis, autoimmune disease or malignancy and no concurrent steroid or immunosuppressive drugs.

PROTOCOL OUTLINE: Randomized study.

Arm I: No further treatment.

Arm II: Single-agent Immunotherapy. BCG-Connaught, BCG, NSC-116341.

Arm III: Single-agent Immunotherapy. Levamisole, LEV, NSC-177023.

Arm IV: 2-agent Combination Immunotherapy. BCG/LEV.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Protein, albumin electrophoresis, whole lung tomograms, liver, brain and bone scan, skin test for recall antigens.

END POINTS: Response/remission rate, duration of response, duration of survival.

CURRENT STATUS: 520 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: No therapy. Patients who relapse are treated at the discretion of the investigator.

Arm II: BCG - 40 mg once a week for 1 month then q month for 36 months. Treat patients who relapse at the discretion of the investigator.

Arm III: LEV - 2.5 mg/kg po on days 1 and 2. Repeat once a week for 36 months. Treat patients who relapse at the discretion of the investigator.

Arm IV: BCG as in Arm II for 8 weeks, alternating with LEV - as in Arm III, for 8 weeks, for a total of 36 months.

Follow all patients q 3 months for the first 36 months, then q 6 months for 24 months then q 12 months for a minimum of 5 years.

Dosage modifications for toxicity are given for BCG only.

DOSAGE FORMS: BCG - 40 mg vials; LEV - not given.

DATE SUMMARIZED: 11/78

9.0061 CHEMOTHERAPY WITH DTIC VS IMMUNOTHERAPY WITH LEVAMISOLE IN HIGH-RISK PATIENTS FOLLOWING EXCISION OF PRIMARY SKIN MELANOMA

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PROTOCOL NUMBER(S) EORTC-18761

OBJECTIVES:

I. Evaluate the effect of chemotherapy with DTIC or immunotherapy with levamisole after surgical removal of primary malignant melanoma of the limbs, trunk or head and neck, with unfavorable histological type, with respect to length of disease-free interval between surgery and recurrence of metastasis, length of survival and undesirable effects.

PROTOCOL ENTRY CRITERIA: Patients between 15 and 75 years who have a previously untreated histologically confirmed primary cutaneous malignant melanoma of Clark's Grade 3 with a thickness equal to or exceeding 1.5 mm, or Grades 4 and 5, without histological evidence of lymph nodal metastases or clinical evidence of visceral metastases. Patients must have had any prior surgery within 1.5 month of study entry, they must not have had any other therapy and must not be receiving immuno-suppressive drugs.

PROTOCOL OUTLINE: Randomized study.

All patients initially undergo surgery for total excision of tumor with a minimum clearance of 3 cm laterally and with intact underlying fascia.

Arm I: Single-agent Chemotherapy. DTIC, NSC-45388.

Arm II: Immunotherapy. Levamisole, LEV, NSC-177023.

Arm III: Control group. Placebo.

STRATIFICATION BY: Clark's Grades 3 and 4 or 5, sex, participating institutions, tumor sites.

SPECIAL STUDY PARAMETERS: Liver scintigraphy, skeleton scintigraphy and/or radiography, EEG and/or brain scintigraphy and immunocompetence tests if possible; LFT.

END POINTS: Disease-free interval, response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response.

CURRENT STATUS: About 228 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Chemotherapy. DTIC - 250 mg/sqm/day iv for days 1 through 5 q 28 days for a total of 6 cycles or until relapse or metastasis.

Arm II: Immunotherapy. LEV - 150 mg/day po for patients under 70 kg, 200 mg/day for patients between 71 and 90 kg and 250 mg/day for patients over 90 kg, given in 3 divided doses (morning, lunch and evenings) for 2 consecutive days every week. Continue therapy for 2 years or until relapse or metastasis.

Arm III: Placebo - same number of tablets, given on same schedule as Arm III therapy, for 2 years or until relapse or metastasis.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: DTIC - not given; LEV - 50 mg tablets.

DATE SUMMARIZED: 06/79

PATIENT ACCRUAL: 01201278

9.0062 LONG-TERM IMMUNOTHERAPY COMPARING TWO BCG PREPARATIONS FOR STAGE I HIGH-RISK MALIGNANT MELANOMA OF THE LIMBS

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PROTOCOL NUMBER(S) EORTC-18781

OBJECTIVES:

I. Evaluate the effect of long-term (3 years) BCG immunotherapy with 2 different types of well characterized BCG in terms of length of disease-free interval, appearance of metastases, length of survival and occurrence of undesirable side effects in patients with surgically removed primary Stage I malignant melanoma (primary tumor without lymph node and/or visceral metastases) of the limbs.

PROTOCOL ENTRY CRITERIA: Patients between the ages of 15 and 75 with previously untreated, histologically confirmed primary cutaneous malignant melanoma of Clark Grade 3 (with a thickness equal to or exceeding 1.5 mm) or of Clark Grades 4 and 5 (irrespective of thickness) who have no clinical evidence of lymph node involvement, visceral metastases or satellites. Patients must not have had a previous malignant tumor or have a coexisting second malignant tumor (except basal cell carcinoma of the skin or in situ cervix carcinoma). Patients must not have a history of major allergic or autoimmune disease.

PROTOCOL OUTLINE: Randomized study. Patients are randomized following Surgery.

Regimen A: Surgery. Wide excision of tumor.

Arm I: BCG Pasteur, BCG, NSC-B116328.

Arm II: BCG R.I.V., a preparation from The Netherlands, no NSC number.

Arm III: No further treatment.

STRATIFICATION BY: Clark grade: 3 (thickness at least 1.5 mm), 4 or 5.

SPECIAL STUDY PARAMETERS: Determination of pretreatment levels of antibodies against a.o. BCG, PPD skin test, chest x-ray, liver blood tests.

END POINTS: Disease-free interval, survival, time of recurrence, adverse reactions.

CURRENT STATUS: A minimum of 228 patients must be entered. As of July 1979, 20 patients have been entered.

DOSAGE SCHEDULE:

Regimen A: Surgery. Totally excise the tumor down to the fascia with a minimum clearance of 3 cm laterally (measured from the outer edge). The underlying fascia should be left intact.

Arm I: Beginning within 4 weeks of Surgery, BCG Pasteur - 3.8 x 10 to the eighth culturable particles (one half of an ampule) in 0.5 ml of isotonic saline is placed on the skin and administered with a multipuncture instrument with 20 needles at a depth setting of 2 mm. BCG is applied first to the affected limb and then to all 4 extremities in a clockwise sequence. BCG is given weekly for 10 weeks, thereafter q 4 weeks for a total of 3 years of therapy.

Arm II: BCG R.I.V. - 6.4 x 10 to the seventh culturable particles (one ampule) administered by the multipuncture technique described in Arm I, weekly for 10 doses, thereafter q 4 weeks for a total of 3 years of therapy.

Arm III: Observation only following Surgery.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG Pasteur - 7.6 x 10 to the eighth culturable particles per ampule; BCG R.I.V. - 6.4 x 10 to the seventh culturable particles per ampule.

DATE SUMMARIZED: 12/80

9.0063 PHASE II CHEMOTHERAPY WITH DAVA FOR ADVANCED (STAGE III) MELANOMA

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PROTOCOL NUMBER(S) EORTC-18792

OBJECTIVES:

I. Assess the antitumor activity of vindesine in advanced, metastatic, malignant melanoma refractory to conventional chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven, advanced, metastatic, malignant melanoma who are not candidates for conventional chemotherapy. Patients must have a minimum life expectancy of 2 months or a minimum performance status of 3. Patients with prior radiotherapy or chemotherapy should have been allowed to recover, as far as is possible, from any toxic effects before beginning protocol treatment.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Measurement of lesions: photographic record, xero-radiography, chest x-ray, tomograms, clinical measurement of liver; hematologic function tests.

END POINTS: Response/remission rate, objective tumor response.

CURRENT STATUS: Between 30 and 100 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 3 mg/sqm iv bolus once a week. Patients who have received more than 6 weeks of prior chemotherapy receive 2 mg/sqm of DAVA. After 6 courses, patients with progressive disease go off study; responders continue treatment, receiving DAVA every 2 or 3 weeks. Patients who develop untoward toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

9.0064 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED MALIGNANT MELANOMA

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PROTOCOL NUMBER(S) EORTC-18793

OBJECTIVES:

I. Assess the objective antitumor activity of PALA in advanced malignant melanoma not previously treated with chemotherapy.

II. Characterize further the pattern of toxic effects of PALA.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with histologic evidence of advanced malignant melanoma with measurable lesions who have received no prior chemotherapy. Patients must have adequate renal function, normal liver function, and favorable hematologic status. Patients with abnormal liver function due to liver metastases are eligible. Patients must have a Karnofsky performance status under 50, and have no CNS metastases, active uncontrolled infection, overt psychosis, or marked senility.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematocrit or hemoglobin, WBC and differential, platelet count, renal and hepatic function tests, chest x-rays, bone scan.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: Initially 20 patients will be treated; 5 patients will be added for each response seen in the first 20.

DOSAGE SCHEDULE:

PALA - 2.5 g/sqm iv infusion over 60 minutes on days 1 and 2 q 2 weeks. Patients with tumor regression continue treatment until tumor progression. Patients showing no change after 6 courses go off study. Patients who develop severe toxicity, despite a 50 percent dose reduction, go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 1 g ampules.

DATE SUMMARIZED: 10/80

9.0065 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED MALIGNANT MELANOMA

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PROTOCOL NUMBER(S) EORTC-18801

OBJECTIVES:

I. Assess the single-agent activity of m-AMSA in advanced malignant melanoma.

II. Define the clinical tolerance to the drug.

PROTOCOL ENTRY CRITERIA: Patients with histologic evidence of advanced, malignant melanoma and measurable or evaluable lesions. Patients must be under 75 years of age and have adequate hematologic status, renal and hepatic function, and a Karnofsky performance status of at least 50. Patients with prior chemotherapy must have recovered from drug-induced toxic effects and have evolutive disease. Patients must not have CNS metastases, uncontrolled infection, psychosis, marked senility, or another malignancy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic function tests, chest x-ray, bone scan, renal and hepatic function tests.

END POINTS: Response/remission rate, duration of response, disease-free interval, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: Initially 20 patients will be entered. For each response seen in the first 20 patients treated, 5 patients will be added.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv over 60 minutes, q 3 weeks, if leukocyte and platelet counts have returned to normal. Patients with progressive disease after 2 courses go off study; all others continue until disease progression or unmanageable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 08/80

9.0066 PHASE II COMBINATION CHEMOTHERAPY WITH CACP/DAVA FOR ADVANCED MALIGNANT MELANOMA

Rozencweig, M., (Brussels (02) 538-65-33) European Org. for Research on Treatment of Cancer, Melanoma Cooperative Group, Institut Jules Bordet, 1 Rue Heger Bordet, 1000 Brussels, Belgium
PROTOCOL NUMBER(S) EORTC-18802

OBJECTIVES:

I. Assess the antitumor activity of a combination of cis-platinum and vindesine in advanced malignant melanoma.

II. Define the clinical tolerance to this regimen.

PROTOCOL ENTRY CRITERIA: Patients with histologic evidence of advanced malignant melanoma and measurable or evaluable lesions (pleural effusion, ascites, and osseous metastases are not considered as measurable lesions). Patients must be under 75 years of age; they must have adequate hematologic, renal, and hepatic function and a Karnofsky performance status of at least 50. Patients must not have CNS metastases, uncontrolled infection, psychosis, marked senility, or another malignancy. Patients with prior chemotherapy must have recovered from any drug-induced toxic effects and have evolutive disease.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Vindesine, DAVA, NSC-245467; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements; chest x-ray; bone scan; hematologic, renal, and hepatic function tests.

END POINTS: Response/remission rate, duration of response, disease-free interval, toxicity/morbidity of treatment, objective tumor response, survival rate.

CURRENT STATUS: 20 patients will be entered initially. For each response seen in the first group, 5 patients will be added.

DOSAGE SCHEDULE:

Chemotherapy is given in 4-week courses. CACP - 100 mg/sqm iv in a 24-hour infusion on day 1, with dextrose prehydration, dextrose and mannitol diuresis over 6 hours, and dextrose hydration over the remaining 18 hours; DAVA - 3 mg/sqm iv rapid infusion given immediately prior to CACP on day 1 and given alone on days 8 and 15. Beginning with the 3rd course, DAVA is given on days 1 and 15 only. All patients are evaluated after 2 courses; those with progressive disease go off study, and all others continue until progressive disease or unmanageable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

9.0067 CHEMOTHERAPY WITH BCNU/ACT-D/DTIC/VCR WITH OR WITHOUT IMMUNOTHERAPY WITH BCG/C. PARVUM FOR VISCERAL OR INOPERABLE METASTATIC MELANOMA

Jacquillat, C., (Paris 200.08.46) Hopital St. Louis, Chemotherapy Unit, 2 Pl. du Docteur Fournier, 75475 Paris 10, France

PROTOCOL NUMBER(S) FRE-UNCHIM-5NK76

OBJECTIVES:

1. Compare combination chemotherapy with BCNU/ACT-D/DTIC/VCR with vs. without immunotherapy with BCG/C. parvum for the treatment of malignant melanoma with visceral metastases or with inoperable metastatic nodes.

PROTOCOL ENTRY CRITERIA: Patients previously untreated with BCNU, ACT-D or VCR with melanoma with visceral metastases of all localization or inoperable node metastases. Patients may have been previously treated by protocol 4NK76.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. BCNU, NSC-409962; Actinomycin-D, ACT-D, NSC-3053; DTIC, NSC-45388; Vincristine, VCR, NSC-67574.

Arm II: 4-Drug Combination Chemotherapy plus Immunotherapy. BCNU/ACT-D/DTIC/VCR; BCG-Pasteur, BCG, NSC-B116328; C. parvum-Merieux, C. parvum, NSC-197213.

STRATIFICATION BY: Participating institutions; previous treatment: systemic Chemotherapy or intra-arterial DTIC; main metastatic localization: liver, lung, brain, nodes, etc.; sex.

SPECIAL STUDY PARAMETERS: Skin tests.

END POINTS: Decrease or increase of metastases, survival rate, toxicity/morbidity of treatment, response rate.

CURRENT STATUS: 22 patients have been entered in two years.

DOSAGE SCHEDULE:

Arm I: BCNU - 150 mg/sqm iv on day 1; ACT-D - 0.3 mg/sqm iv on day 1; DTIC - 400 mg/sqm iv on days 8, 15 and 22; VCR - 0.6 mg/sqm iv on days 8, 15 and 22. Repeat course q 4 weeks.

Arm II: BCNU, ACT-D, DTIC, VCR, as in Arm I; plus BCG - 0.1 mg id in both axillas and both groin areas on day 1; C. parvum - 2 ml sc on days 1, 8, 15 and 22. Repeat course q 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; ACT-D - 0.5 mg vials; DTIC -200 mg vials; VCR - 1 mg ampules; BCG lyophilysate - 0.5 ml ampules; C. parvum - 2 ml ampules.

DATE SUMMARIZED: 06/78

9.0068 ADJUVANT BCNU/ACT-D/DTIC/VCR CHEMOTHERAPY WITH OR WITHOUT BCG/C. PARVUM IMMUNOTHERAPY FOR MELANOMA WITH METASTATIC NODES

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PROTOCOL NUMBER(S) FRE-UNCHIM-7NK76

OBJECTIVES:

1. Compare combination chemotherapy with BCNU/ACT-D/DTIC/VCR with vs. without BCG/C. parvum immunotherapy for the postsurgical treatment of malignant melanoma with metastatic nodes.

PROTOCOL ENTRY CRITERIA: Patients previously untreated with BCNU, ACT-D or VCR with operable metastatic nodes of malignant melanoma that have undergone surgical resection. Patients must be free of local recurrence or visceral metastasis, and may have had prior treatment on protocol 4NK76.

PROTOCOL OUTLINE: Randomized study. Enter all patients within 30 days following surgery.

Arm I: 4-Drug Combination Chemotherapy. BCNU, NSC-409962; Actinomycin-D, ACT-D, NSC-3053; DTIC, NSC-45388; Vincristine, VCR, NSC-67574.

Arm II: 4-Drug Combination Chemotherapy plus Immunotherapy. BCNU/ACT-D/DTIC/VCR, plus BCG-Pasteur, BCG, NSC-B116328; plus C. parvum-Merieux, C. parvum, NSC-197213.

STRATIFICATION BY: Previous treatment: systemic Chemotherapy or intra-arterial DTIC; sex.

SPECIAL STUDY PARAMETERS: Skin tests.

END POINTS: Disease-free interval, development of new metastases, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 78 patients were entered in two years.

DOSAGE SCHEDULE:

Arm I: BCNU - 150 mg/sqm iv on day 1; ACT-D - 0.3 mg/sqm iv on day 1; DTIC - 400 mg/sqm iv on days 1 and 15; VCR - 0.6 mg/sqm iv on days 1 and 15. Repeat course q 4 weeks, up to 12 months.

Arm II: BCNU/ACT-D/DTIC/VCR, as in Arm I; plus BCG - 0.1 ml id in both axillas and both groin areas on day 1; C. parvum - 2 ml sc on days 1 and 15. Repeat course q 4 weeks, up to 18 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; ACT-D - 0.5 mg vials; DTIC -200 mg vials; VCR - 1 mg ampules; BCG lyophilosates - 0.5 ml ampules; C. parvum - 2 ml ampules.

DATE SUMMARIZED: 06/78

9.0069 LOCAL IMMUNOTHERAPY WITH BCG WITH OR WITHOUT CHEMOTHERAPY WITH BCNU/ACT-D/DTIC/VCR FOR SKIN METASTASES OF MALIGNANT MELANOMA

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PROTOCOL NUMBER(S) FRE-UNCHIM-9NK76

OBJECTIVES:

I. Compare intratumoral inoculation of BCG with vs. without 4-drug combination systemic chemotherapy for the treatment of skin metastases of malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients previously untreated with BCNU, ACT-D or VCR with skin metastases of malignant melanoma in transit (i.e., located between the primary and the main regional lymph nodes). Patients may have been previously treated on protocol 4NK76.

PROTOCOL OUTLINE: Randomized study.

Arm I: Intratumoral Immunotherapy. BCG-Pasteur, BCG, NSC-B116328.

Arm II: Intratumoral Immunotherapy plus 4-Drug Combination Systemic Chemotherapy. BCG; plus BCNU, NSC-409961; Actinomycin-D, ACT-D, NSC-3053; DTIC, NSC-45388; Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Prior therapy: systemic chemotherapy or intra-arterial DTIC; sex.

SPECIAL STUDY PARAMETERS: Evolution of metastatic skin tumors, skin tests.

END POINTS: Appearance of lymph nodes metastases or visceral metastases, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 6 patients have been entered in two years.

DOSAGE SCHEDULE:

Arm I: BCG - 0.1 ml intratumoral inoculation in each lesion, q 7 days up to complete regression of skin nodules.

Arm II: Local BCG Immunotherapy - as in Arm I; plus BCNU - 150 mg/sqm iv on day 1; ACT-D - 0.3 mg/sqm iv on day 1; DTIC - 400 mg/sqm iv on days 1 and 15; VCR - 0.6 mg/sqm iv on days 1 and 15. Repeat course q 4 weeks up to 12 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; ACT-D - 0.5 mg vials; DTIC -200 mg vials; VCR - 1 mg ampules; BCG lyopholisate - 0.5 ml ampules.

DATE SUMMARIZED: 06/78

9.0070 MER-BCG IMMUNOTHERAPY WITH AND WITHOUT DTIC CHEMOTHERAPY FOR MALIGNANT MELANOMA

Robinson, E., Israel Institute of Technology, RAMBAM Medical Center, Dept. of Oncology and Nuclear Medicine, Haifa, Israel
PROTOCOL NUMBER(S) ISR-MEL-1

OBJECTIVES:

I. Determine the effect of adjuvant MER-BCG (MER) alone or combined with DTIC in patients with malignant melanoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven, radically resected, malignant melanoma Stages I and II. Surgery must have been performed 10-30 days prior to entry.

PROTOCOL OUTLINE: Randomize Stage I patients to Arms I, II; Stage II patients to Arms III, IV.

Arm I: Immunotherapy. MER-BCG, MER, NSC-143769.

Arm II: No further treatment.

Arm III: Immunotherapy. MER as in Arm I.

Arm IV: Immunotherapy plus Single-agent Chemotherapy. MER plus DTIC, NSC-45388.

STRATIFICATION BY: Age, sex, disease stage.

SPECIAL STUDY PARAMETERS: Skin tests for recall antigens, lymphocyte stimulation tests.

END POINTS: Recurrence rate, length of survival.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

Arm I: MER - dosage and route of administration not given, but dependent upon individual skin reactivity.

Arm III: MER - as in Arm I.

Arm IV: MER - as in Arm I. DTIC - 250 mg/sqm/day for 5 days q 3 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

9.0071 RANDOMIZED TRIAL OF INTRALYMPHATIC BCG FOLLOWING EXCISION OF PRIMARY MELANOMA OF LOWER EXTREMITIES WITHOUT REGIONAL NODE INVOLVEMENT

Veronesi, U., (Milano 02-2390) Istituto Nazionale Tumori, Via Venezian, 20133 Milano, Italy
PROTOCOL NUMBER(S) ITA-IGM-9

OBJECTIVES:

I. Evaluate in a randomized trial the effect of postoperative intralymphatic administration of BCG in patients undergoing wide excision of primary lower extremity melanoma without metastases to the regional nodes.

PROTOCOL ENTRY CRITERIA: Patients with primary melanoma confined to the lower extremities without metastases to the regional nodes. There may be no history of prior immunotherapy, and primaries may not be located in sites other than the lower extremities.

PROTOCOL OUTLINE: Randomized study.

Regimen A. Surgery.

Arm I: Immunotherapy. BCG-Pasteur, BCG, NSC-B116328.

Arm II: No further treatment.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Survival, incidence of regional node metastasis.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Wide excision of primary.

Arm I: BCG - 2 mg of lyophylized BCG administered intralymphatically.

Arm II: Observation only.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by the investigator.

DATE SUMMARIZED: 12/80

SECTION 10

SARCOMA

10A. OSTEOGENIC SARCOMA AND OTHER BONE TUMORS

CCG-741	PHASE III CHEMOTHERAPY WITH HIGH-DOSE VS MODERATE-DOSE MTX PLUS VCR/ADR AND CF FOR PRIMARY AND METASTATIC OSTEOGENIC SARCOMA	10.0001
RTOG-7810	PHASE I/II STUDY OF HALF-BODY RADIOTHERAPY FOR MULTIPLE OSSEOUS METASTASES	10.0002
SWOG-7906	PHASE III MULTIDRUG ADJUVANT CHEMOTHERAPY IN NON-METASTATIC OSTEOSARCOMA CONPADRI-1 (CTX/VCR/L-PAM/ADR) VS COMPADRI-V (CONPADRI-1/MTX)	10.0003
MAYO-767601	POSTSURGICAL ADJUVANT CHEMOTHERAPY WITH CTX, ADR, VCR, MTX AND CF FOR OSTEOGENIC SARCOMA AND OTHER SARCOMAS OF BONE	10.0004
MDAR-200	ADJUVANT CHEMOTHERAPY WITH CONPADRI (ADR/VCR/CTX/L-PAM) FOR ADULT OSTEOSARCOMA	10.0005
MDAR-55	CHEMOTHERAPY WITH VCR/MTX/CITROVORUM RESCUE AND RADIOTHERAPY FOR PULMONARY METASTASES FROM OSTEOGENIC SARCOMA	10.0006
NCI-77-C-180	SURGERY OR 6- VS 42-HOUR HIGH-DOSE MTX FOLLOWED BY INTENSIVE CHEMOTHERAPY FOR METASTATIC OSTEOSARCOMA	10.0007
ARG-SAO-7804	PILOT STUDY OF ADJUVANT THERAPY WITH ADRIAMYCIN/CIS-PLATINUM FOR OSTEOGENIC SARCOMA	10.0008
EORTC-20781	MTX/CF/VCR CHEMOTHERAPY ALTERNATING WITH ADR/CTX PLUS RADIOTHERAPY VS CHEMOTHERAPY OR RADIOTHERAPY ALONE FOR OSTEOSARCOMA	10.0009
EORTC-62782	HIGH-DOSE MTX VS LOW-DOSE MTX CHEMOTHERAPY FOR ADVANCED OSTEOSARCOMA	10.0010
EORTC-62794	PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR ADVANCED OSTEOGENIC SARCOMA	10.0011
UICC-76052	ADJUVANT PROPHYLACTIC COMBINATION CHEMOTHERAPY WITH VCR/MTX/CF/ADR OR VCR/MTX/CF FOR OCCULT LUNG METASTASES IN OSTEOSARCOMA	10.0012

10B. SOFT TISSUE SARCOMA

EST-PA-380	PHASE II CHEMOTHERAPY WITH AMSA FOR MALIGNANT MESOTHELIOMA OF THE PLEURAL OR PERITONEAL CAVITY	10.0013
EST-2377	ADJUVANT CHEMOTHERAPY WITH ADRIAMYCIN FOR SOFT TISSUE SARCOMA	10.0014
SWOG-7765	PHASE I-II PILOT CHEMOTHERAPY WITH ADRIAMYCIN/DTIC FOR SOFT TISSUE SARCOMAS	10.0015
BCRP-7906	COMBINATION CHEMOTHERAPY WITH ADR/CTX PLUS WHOLE BODY HYPERTHERMIA FOR METASTATIC SOFT TISSUE SARCOMA	10.0016

BCRP-8016 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE (DHAD) FOR METASTATIC SOFT TISSUE SARCOMA 10.0017
MDAR-379 CHEMOTHERAPY WITH CTX PLUS CONTINUOUS INFUSION OF ADR AND DTIC FOR METASTATIC OR UNRESECTABLE SOFT TISSUE SARCOMA 10.0018
MSKCC-7962 VAC (VCR/CTX/ADR) COMBINATION CHEMOTHERAPY WITH & WITHOUT MIXED BACTERIAL VACCINE IMMUNOTHERAPY AS ADJUVANT TREATMENT OF SOFT TISSUE SARCOMA 10.0019
MTS-2 CHEMOTHERAPY WITH ADRIAMYCIN PLUS RADIOTHERAPY FOLLOWED BY 5-AZACYTIDINE FOR MALIGNANT MESOTHELIOMA 10.0020
NCI-76-C-191 RADICAL SURGERY AND CHEMOTHERAPY VS CONSERVATIVE SURGERY AND RADIOTHERAPY WITH/WITHOUT CHEMOTHERAPY FOR SOFT TISSUE SARCOMA OF THE EXTREMITIES 10.0021
NCI-76-C-192 SURGERY PLUS RADIOTHERAPY PLUS ADR/CTX FOLLOWED BY MTX VS SURGERY PLUS RADIOTHERAPY ALONE FOR SOFT TISSUE SARCOMA OF THE HEAD, NECK, OR TRUNK 10.0022
NCI-78-C-182 EVALUATION OF CHEMOTHERAPY WITH ADR/CTX AND MTX AS ADJUVANT THERAPY IN PATIENTS RECEIVING RADIOTHERAPY FOR SOFT TISSUE SARCOMA 10.0023
NCI-80-C-45 EVALUATION OF INTRAOPERATIVE RADIOTHERAPY & ADJUVANT CHEMOTHERAPY WITH CAM (CTX/ADR/MTX) FOR SOFT TISSUE RETROPERITONEAL SARCOMA 10.0024
SFCC-78060 PHASE III CHEMOTHERAPY WITH ADRIAMYCIN FOR SOFT TISSUE SARCOMA STAGES IIIB THROUGH IVA 10.0025
ARG-LACRIP-7 CHEMOTHERAPY WITH CYVADIC (CTX/VCR/ADR/DTIC) VS ADR/DTIC/CACP FOR ADVANCED SOFT TISSUE SARCOMAS 10.0026
EORTC-62761 COMBINATION CHEMOTHERAPY WITH ADR/DTIC/CTX/VCR FOR METASTATIC SOFT TISSUE SARCOMA 10.0027
EORTC-62771 SURGERY WITH VS WITHOUT ADJUVANT CHEMOTHERAPY WITH ADR/DTIC/CTX/VCR FOR SOFT TISSUE SARCOMA 10.0028
EORTC-62793 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED REFRACTORY SOFT TISSUE SARCOMA 10.0029
EORTC-62802 PHASE II CHEMOTHERAPY WITH ADRIAMYCIN VS CARMINOMYCIN FOR ADVANCED SOFT TISSUE SARCOMA 10.0030

10C. SARCOMA—GENERAL

EST-1379 MASTER PROTOCOL AND PHASE II CHEMOTHERAPY WITH BLEO VS CLZ AND MGBG VS BRUCEANTIN FOR ADVANCED SOFT-TISSUE AND BONE SARCOMAS AND MESOTHELIOMAS 10.0031
EST-3377 PHASE III CHEMOTHERAPY WITH ADR AND/OR PHASE II CHEMOTHERAPY WITH DBD, MTS OR ICRF-159 FOR SOFT TISSUE AND BONE SARCOMA AND MESOTHELIOMA 10.0032
SEG-SAR-P27 PILOT STUDY OF COMBINATION CHEMOTHERAPY WITH ADRIAMYCIN/CYCLOPHOSPHAMIDE/DTIC FOR METASTATIC SARCOMA 10.0033
SEG-78SAR0103 CHEMOTHERAPY WITH ADR/CTX/MTX VS ADR/CTX/MTX/AMPHOTERICIN-B & MAINTENANCE WITH ACT-D VS ACT-D/AMPHOTERICIN-B FOR METASTATIC SARCOMA 10.0034
SWOG-7982 PHASE II CHEMOTHERAPY WITH CHLOROZOTOCIN FOR ADVANCED SARCOMA 10.0035
SWOG-8004 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE FOR SOFT TISSUE AND BONE SARCOMA 10.0036
MAYO-797701 PHASE II INDUCTION WITH BLEO/CTX/ADR/CACP AND CONSOLIDATION WITH ALTERNATING VCR/CTX/ACT-D AND VCR/ADR/DTIC FOR ADVANCED SARCOMAS 10.0037
MDAR-271 PHASE II CHEMOTHERAPY WITH AMSA FOR REFRACTORY METASTATIC SARCOMA 10.0038

MDAR-331 PHASE II CONTINUOUS 5-DAY INFUSION CHEMOTHERAPY WITH DAVA VS VBL FOR REFRACTORY METASTATIC SARCOMA 10.0039

MDAR-396 PHASE II CHEMOTHERAPY WITH PALA FOR REFRACTORY METASTATIC SARCOMA 10.0040

MDAR-417 PHASE II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR ADVANCED SOFT TISSUE AND BONE SARCOMA 10.0041

NCI-78-C-101 PRIMARY RADIOTHERAPY AND RADIOSENSITIZATION WITH MISONIDAZOLE FOR UNRESECTABLE OSTEOGENIC SARCOMA AND CHONDROSARCOMA 10.0042

UCLA-SAR-1 CHEMOTHERAPY WITH ADR, MTX WITH & WITHOUT ADJUVANT IMMUNOTHERAPY WITH BCG & ALLOGENEIC TUMOR CELL VACCINE IN SKELETAL & SOFT TISSUE SARCOMA 10.0043

SECTION 10

SARCOMA

10A. OSTEOGENIC SARCOMA AND OTHER BONE TUMORS

10.0001 PHASE III CHEMOTHERAPY WITH HIGH-DOSE VS MODERATE-DOSE MTX PLUS VCR/ADR AND CF FOR PRIMARY AND METASTATIC OSTEOGENIC SARCOMA

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-741

OBJECTIVES:

I. Compare the effects of combination chemotherapy with adriamycin, vincristine, and high-dose vs. moderate-dose methotrexate with citrovorum factor rescue on recurrence, metastases, and survival in patients with primary or metastatic osteogenic sarcoma.

II. Evaluate toxicity of these regimens, prognostic factors, effect of immunologic status and incidence of certain HLA types.

PROTOCOL ENTRY CRITERIA: Post-surgical (biopsy or primary resection) patients with primary or metastatic osteosarcoma, without prior chemotherapy unless metastatic disease is present.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy plus Radiotherapy. Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; high-dose Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590.

Arm II: 4-Drug Combination Chemotherapy plus Radiotherapy. ADR, VCR, moderate-dose MTX, CF.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Plasma MTX level radioassay, immunological studies, bone scan q 3 months (Addendum 2, March 1977).

END POINTS: Recurrence rate, disease-free interval, appearance of metastases, survival rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: (Addendum 5, August 1978) ADR - 30 mg/sqm iv at surgery followed by 30 mg/sqm iv for 3 days q 6 weeks for 6 courses (maximum cumulative dose 600 mg/sqm). VCR - 2 mg/sqm iv given 30 minutes following MTX. MTX -6000 mg/sqm iv given over 6 hours at 3 weeks post surgery, followed by 7500 mg/sqm (route not stated) given over 6 hours at 9 weeks and q 6 weeks thereafter for 11 doses. CF - 12 mg iv q 3 hours for 8 doses beginning 2 hours after MTX, followed by 12 mg po q 6 hours for 8 doses. Continue therapy for 18 months. Radiotherapy: 3 split course doses of 2000 rad each given on days 49 through 63, 70 through 84 and 91 through 105 to primary tumor site. Radiotherapy to metastatic sites may be given at the same time.

Arm II: Radiotherapy as in Arm I plus Chemotherapy with ADR, VCR, as in Arm I, plus MTX - 690 mg/sqm given in 42 hours 3 weeks after surgery and q 6 weeks thereafter for 11 more doses. CF - 12 mg/sqm iv q 6 hours for 7 doses following MTX therapy.

Maintain diuresis and urinary alkalinization during all MTX/CF therapy.

DATE SUMMARIZED: 02/79

PATIENT ACCRUAL: 00900279

10.0002 PHASE I/II STUDY OF HALF-BODY RADIOTHERAPY FOR MULTIPLE OSSEOUS METASTASES

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7810

OBJECTIVES:

I. Evaluate the frequency and the duration of pain relief as a function of the dose schedules proposed.

II. Assess tumor and response by evaluation of measurable lesions in different sites.

III. Determine the normal tissue tolerance and toxicity following single exposure doses of irradiation, particularly focusing on the dose-limiting organs: bone marrow, lung, kidney, liver, brain, spinal cord, small bowel and heart, both in terms of acute and late reactions and damage.

IV. Study the natural history of progression of disseminated cancer, particularly the osseous lesions, and develop a useful staging system for evaluation of disseminated disease.

PROTOCOL ENTRY CRITERIA: Patients not over 70 years of age with painful, multiple bony metastases documented by radiographs and/or bone scans in either femora, humi, ribs, pelvis or cervical, dorsal or lumbar vertebrae. Patients must not have symptomatic or painful multiple organ metastases on the side of the body not to be irradiated. Patients must have adequate bone marrow, hepatic, renal and pulmonary function, a life expectancy of at least 3 months and a pain or narcotic score or 4. Patients must not have a histologic diagnosis of lymphoma, leukemia or multiple myeloma and must not have had previous half-body irradiation to the half of the body to be treated with this protocol.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Megavoltage with photon energies higher than 1 MeV including Cobalt-60, 2 MeV X-rays, 4 MeV linear accelerator or greater.

STRATIFICATION BY: Primary tumor type: breast vs. lung vs. prostate vs. other; sites of bony metastases: femur and humerus vs. pelvis vs. spine vs. ribs; extent of multiple metastases: osseous sites only vs. osseous plus other sites.

SPECIAL STUDY PARAMETERS: Tests of renal, pulmonary and hepatic function, bone, brain, liver, and soft tissue scans, SMA-6, SMA-12.

END POINTS: Response/remission rate, objective tumor response, pain relief, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Enter cohorts of 25 to 30 patients for treatment to the most involved half of the body. Dosages are assigned by RTOG Headquarters: 600, 700 or 800 rads single dose to upper half of the body, or 800, 900 or 1000 rads single dose to lower half or middle segment of the body. Dose rates are 15 to 40 rads/minute. Upper-half-body Radiotherapy requires correction for total lung dosage, premedication and 24-hour hospitalization. Allow 6 to 8 weeks for bone marrow recovery, if other half of body is to be irradiated (as a separate protocol entry).

Evaluate after 14 days; if there is no relief, give additional local treatment and consider patient a treatment failure. Follow up all patients for fracture and disease natural history.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/78

10.0003 PHASE III MULTIDRUG ADJUVANT CHEMOTHERAPY IN NON-METASTATIC OSTEOSARCOMA CONPADRI-1 (CTX/VCR/L-PAM/ADR) VS COMPADRI-V (CONPADRI-1/MTX)

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7906

OBJECTIVES:

I. Compare disease-free survival in patients with non-metastatic osteosarcoma treated with CONPADRI-I: cyclophosphamide (CTX), vincristine (VCR), phenylalanine mustard (L-PAM), and adriamycin (ADR), with those treated with COMPADRI-V: high-dose methotrexate (MTX) with citrovorum factor/CONPADRI-I.

II. Determine prognostic differences in the subtypes of osteogenic sarcoma.

III. Evaluate the effect of pre-operative high-dose methotrexate on the amputation specimen in patients on the COMPADRI-V arm.

PROTOCOL ENTRY CRITERIA: Patients with histologically established diagnosis of osteosarcoma without metastases, without previous amputation, who do not require limb salvage procedure. Patients must not have had prior chemotherapy, or evidence of parosteal sarcoma, chondrosarcoma, or fibrosarcoma.

PROTOCOL OUTLINE: Randomized study.

Arm I: Ablative Surgery followed by 4-Drug Combination Chemotherapy. CONPADRI-I: Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Phenylalanine Mustard, L-PAM, NSC-8806; Adriamycin, ADR, NSC-123127.

Arm II: 5-Drug Combination Chemotherapy plus Ablative Surgery. COMPADRI-V: CONPADRI-I plus high-dose Methotrexate, MTX, NSC-740 with Citrovorum Factor, CF, NSC-3590 (HD-MTX-CF).

STRATIFICATION BY: Participating institutions; age: equal to or less than 16 years of age or more than 16.

SPECIAL STUDY PARAMETERS: Lung tomograms, toxicity notations.

END POINTS: Development of metastases or recurrence at amputation site; toxicity/morbidity of treatment.

CURRENT STATUS: 69 patients each arm, annual accrual rate 50 patients.

DOSAGE SCHEDULE:

Arm I: On recovery from Surgery, begin CONPADRI-I. Pediatric: CTX - 10 mg/kg/d x 5, iv weeks 13, 49, and 67; VCR - 0.05 mg/kg iv weekly x 6, weeks 1, 8, 22, 29, 36, and 43; L-PAM - 0.3 mg/kg, iv single doses weeks 31, 43, 61, and 73; ADR - 1.5 mg/kg, iv, single pulse, weeks 1, 4, 7, 19, 22, and 25 and reduced to 1.0 mg/kg on weeks 37, 38, 55, and 56. Adult: CTX - 300 mg/sqm; VCR - 2 mg (maximum dose 2.0 mg); L-PAM - 10 mg/sqm; ADR - 45 mg/sqm, later reduced to 30 mg/sqm. Weekly schedule same as pediatric.

Arm II: COMPADRI-V. All patients receive 6 courses HD-MTX-CF and 6 courses VCR. Surgery at week 9 following recovery from MTX toxicity. Post-surgical Chemotherapy same as CONPADRI-I except for 6 initial doses VCR. Treatment begins at about week 13, when wound is completely healed.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100 and 500 mg ampules; L-PAM - 100 mg vials; ADR - 10 and 50 mg ampules; VCR - 1 and 5 mg ampules; MTX - 500 mg ampules; CF - 3 and 50 mg ampules.

DATE SUMMARIZED: 02/80

10.0004 POSTSURGICAL ADJUVANT CHEMOTHERAPY WITH CTX, ADR, VCR, MTX AND CF FOR OSTEOGENIC SARCOMA AND OTHER SARCOMAS OF BONE

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PROTOCOL NUMBER(S) MAYO-767601

OBJECTIVES:

I. Compare observation alone and high-dose methotrexate with citrovorum rescue for effectiveness in prolonging the initial disease-free survival period in patients who have experienced apparently complete primary excision of classical osteogenic sarcoma and other sarcomas of bone.

II. Attempt complete excision of metastatic tumor, and follow with evaluation of the effectiveness of two chemotherapeutic regimens as adjuvant treatment in patients presenting with metastatic disease and in those who relapse within the initial two postoperative years.

III. Increase the survival of patients who have osteogenic sarcoma, by primary excision with or without chemotherapy or following secondary excision with further adjuvant chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of primary and metastatic classical, high-grade osteogenic sarcoma, atypical osteosarcomas and other sarcomas of bone in surgically accessible sites.

Patients with metastatic lesions appearing within two years of the time of initial diagnosis of primary disease are also eligible if all metastatic lesions can be excised. Patients must not have received prior chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: No active therapy following surgery, unless signs of progressive disease appear.

Arm II: 3-Drug Combination Chemotherapy following surgical removal of all known disease. Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590.

Arm III: 2-Drug Combination Chemotherapy following surgical excision of metastatic disease. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Classical vs. atypical cases - extent of disease, site of primary lesion, histologic grade, histologic type, delayed-type hypersensitivity status, sex and tumor size.

SPECIAL STUDY PARAMETERS: Chest X-ray; whole lung tomogram; skeletal survey; immunologic profile - skin tests, lymphocyte blastogenesis, quantitation of T and B cells, cytotoxicity, monocyte chemotaxis.

END POINTS: Response/remission rate, duration of disease-free interval, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Approximately 200 patients will be entered.

DOSAGE SCHEDULE:

Arm I: No active therapy following surgery. Re-evaluate patients q 6 weeks during the 1st year, and q 12 weeks during the 2nd year. If relapse occurs within two years, randomize such patients to Arm II or Arm III following surgical excision of the recurrent disease (if resectable).

Arm II: Start within 2 to 4 weeks following surgical removal of all known disease. VCR - 2 mg/sqm (maximum), iv, at time 0 followed 1/2 hour later by MTX (high dose) - 3 gm/sqm, iv infusion over a 6-hour period, followed 2 hours after termination of MTX by CF - 15 mg, iv, q 3 hours for 8 doses, then 15 mg q 6 hours for 8 additional doses. Continue therapy on day 22 with MTX (high dose) - 6 gm/sqm, iv, over a 6-hour period, 3 weeks later 7.5 gm/sqm, then 7.5 gm/sqm q 3 weeks for 1 year following surgery. Evaluate patients q 6 weeks during the 1st year and q 12 weeks during the 2nd year. Enter patients with progression to Arm III following total excision of all metastatic lesions.

Arm III: Begin therapy between 2 to 4 weeks following surgical excision of metastatic disease. CTX - 1200 mg/sqm, iv, alternating q 3 weeks with ADR - 75 mg/sqm, iv, for 1 year (maximum cumulative dose of ADR - 540 mg/sqm). Re-evaluate patients q 6 weeks during the 1st year and q 12 weeks during the 2nd year. Enter patients who relapse within 2 years to Arm II following surgical excision if they have not received it previously.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200 and 500 mg vials; MTX - 500 mg vials; CF - 3 mg ampules; ADR and VCR - not given.

DATE SUMMARIZED: 04/77

PATIENT ACCRUAL: 00440279

10.0005 ADJUVANT CHEMOTHERAPY WITH CONPADRI (ADR/VCR/CTX/L-PAM) FOR ADULT OSTEOSARCOMA

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PROTOCOL NUMBER(S) MDAR-200

OBJECTIVES:

I. Evaluate the effectiveness of a combination of drugs as adjunctive chemotherapy in the primary treatment of patients beyond childhood with clinically nonmetastatic osteogenic sarcoma.

II. Determine the efficacy of combination chemotherapy using adriamycin, vincristine, cyclophosphamide and melphalan in preventing the recurrence of and/or metastases of osteosarcoma in a selected number of patients who are clinically tumor-free.

III. Compare the results with those obtained by other treatment modalities.

PROTOCOL ENTRY CRITERIA: Patients with osteogenic sarcoma without metastases who have had no prior chemotherapy. Patients who have undergone amputation must have had the procedure done within 4 weeks prior to treatment with chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. CONPADRI: Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; Melphalan, L-PAM, NSC-8806.

STRATIFICATION: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 20 patients will be entered in 1 year.

DOSAGE SCHEDULE:

ADR - 1.5 mg/kg iv q 3 weeks for 3 courses starting at weeks 0 and 18, then 1.0 mg/kg/week for 2 courses starting at weeks 36 and 54; VCR - 0.05 mg/kg/week iv (maximum 2 mg) for 6 courses starting at week 0, then weekly for 2 courses starting at weeks 12, 30 and 42; CTX - 10 mg/kg/day po for 7 days (maximum 500 mg/day) starting at weeks 12, 48, and 66; L-PAM - 0.3 mg/kg iv single dose at weeks 30, 42, 60 and 72. Omit ADR on appearance of significant EKG abnormalities or other evidence of cardiotoxicity.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/78

10.0006 CHEMOTHERAPY WITH VCR/MTX/CITROVORUM RESCUE AND RADIOTHERAPY FOR PULMONARY METASTASES FROM OSTEOGENIC SARCOMA

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PROTOCOL NUMBER(S) MDAR-55

OBJECTIVES:

I. Study the effectiveness of massive-dose methotrexate with citrovorum factor rescue regimen in combination with radiotherapy in children with pulmonary metastases from osteogenic sarcoma.

II. Evaluate the toxicity and patient tolerance of this regimen.

III. Evaluate how a therapeutic approach of this nature can be combined with a surgical attack on the pulmonary metastases.

PROTOCOL ENTRY CRITERIA: Patients with measurable lesions of metastatic pulmonary osteogenic sarcoma not amenable to surgical treatment, who have had no prior chemotherapy with methotrexate. Patients who have had prior pulmonary radiotherapy will be eligible for methotrexate therapy Arm I and III only and may have had prior massive methotrexate exposure.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: 2-Drug Combination Chemotherapy plus Leucovorin Rescue. Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740. Citrovorum Factor rescue, CF, NSC-3590.

Regimen B: Radiotherapy. Cobalt-60 megavoltage to lungs.

Regimen C: 2-Drug Combination Chemotherapy plus Leucovorin Rescue. Regimen A plus Maintenance with MTX.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: MTX blood levels.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 15 patients will be entered in approximately 18 months.

DOSAGE SCHEDULE:

Regimen A: VCR - 2 mg/sqm (maximum dose 2 mg) route not given, single dose on day 1, followed 24 hours later by MTX - 75 mg/kg as 6-hour iv drip, followed 2 hours later by CF - 15 mg iv q 3 hours for 9 doses, then by CF - 15 mg iv q 6 hours for 8 doses. Repeat VCR on day 22 followed by MTX.

Regimen B: Following last dose of CF, give Radiotherapy - 1500 rads tumor dose given to both lungs over a period of 2 weeks or 2,000 rads to a very localized field over a period of 5 days. Rest 3 weeks.

Regimen C: Repeat Regimen A with VCR, MTX, and CF, with MTX dose at 200 mg/kg. Rest 3 weeks, then repeat course with MTX dose at 250 mg/kg. Continue Maintenance until relapse occurs or for 18 months with VCR, MTX at 250 mg/kg, and with duration of CF rescue dependent on clinical response and MTX blood levels.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/76

10.0007 SURGERY OR 6- VS 42-HOUR HIGH-DOSE MTX FOLLOWED BY INTENSIVE CHEMOTHERAPY FOR METASTATIC OSTEOSARCOMA

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PROTOCOL NUMBER(S) NCI-77-C-180

OBJECTIVES:

I. Examine the difference in tumor response rates and toxicities when high-dose methotrexate is given as a 6-hour bolus infusion vs. a 42-hour infusion in patients with metastatic osteosarcoma.

II. Evaluate the efficacy of intensive chemotherapy in eradicating all microscopic foci of metastatic osteosarcoma in patients in whom there is no clinical evidence of disease.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven metastatic osteosarcoma who have had no prior surgery, chemotherapy, or radiotherapy for their metastases. Patients may have failed earlier adjuvant therapy. Patients must be under the age of 30 and must have no serious concurrent disease. Bone marrow, kidney, and liver function must be adequate.

PROTOCOL OUTLINE: Randomized study for Phase I: Enter all patients who can be rendered NED by surgery to Arm I and randomize others to Arms II and III. Phase II Intensification nonrandomized.

Phase I: Debulking creation of NED.

Arm I: Surgery.

Arm II: 2-Drug Combination Chemotherapy plus Citrovorum Rescue. Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590. MTX in 6-hour infusion.

Arm III: 2-Drug Combination Chemotherapy plus Citrovorum Rescue. VCR; MTX; CF. MTX in 42-hour infusion.

Phase II: Intensification.

Regimen A: Induction: 7-Drug Combination Chemotherapy plus Citrovorum Rescue. VCR; MTX; CF; Adriamycin, ADR, NSC-123127; DTIC, NSC-45388; Cyclophosphamide, CTX, NSC-26271; Melphalan, L-PAM, NSC-8806; cis-Platinum, CACP, NSC-119875.

Regimen B: Maintenance: 3-Drug Combination Chemotherapy plus Citrovorum Rescue. VCR; MTX; CF; ADR.

STRATIFICATION BY: Prior adjuvant chemotherapy (yes vs. no), nature of metastases (amenable to NED by surgery alone vs. not amenable by surgery alone).

SPECIAL STUDY PARAMETERS: Hemogram, coagulation studies, chemistries, EKG, chest x-ray, bone scan, lung tomograms, brain EMI, audiogram.

END POINTS: Response/remission rate, disease-free interval, survival, toxicity/morbidity of treatment.

CURRENT STATUS: At least 20 patients should be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: Remove all visible macroscopic tumor.

Arm II: VCR - 2 mg/sqm (maximum 2 mg) iv; MTX - 3 g/sqm iv over 6 hours; CF - 15 mg/sqm iv q 3 hours for 24 hours, then q 6 hours for 48 hours or until serum MTX is less than 4 x 10 to the minus seventh M, beginning 2 hours after the end of the MTX infusion. Repeat weekly, with subsequent courses containing MTX at 7.5 g/sqm, for a total of 4 courses.

Arm III: VCR - 2 mg/sqm (maximum 2 mg) iv; MTX - 600 mg/sqm iv over 1 hour, then 120 mg/sqm/hour by continuous iv infusion over 41 hours; CF - 96 mg/sqm iv followed at 6-hour intervals by 12 mg/sqm until plasma MTX level is less than 5 x 10 to the minus eighth M. Repeat q 2 weeks.

Minimum MTX treatment will be 4 weeks of therapy. Evaluate at end of 4th week. Patients with NED enter Regimen A; those who could be converted to NED by surgery enter Arm I; those with progressive disease declare failure; continue treatment in other patients until NED or progression.

Regimen A: VCR - 2 mg/sqm iv on day 1; MTX - 7.5 g/sqm iv over 6 hours; CF - 15 mg/sqm iv q 3 hours for 24 hours, then q 6 hours for 48 hours, beginning 2 hours after completion of MTX infusion; ADR - 35 mg/sqm iv on days 8, 9, and 10; DTIC - 250 mg/sqm iv on days 8, 9, 10, 11, and 12; CTX - 40 mg/kg iv on days 8, 9, and 15; L-PAM - 0.4 mg/kg iv on days 15 and 16. Allow for marrow recovery, then ADR - 35 mg/sqm iv on days 1, 2, and 3; CACP - 20 mg/sqm iv over 30 minutes with adequate prehydration and concurrent mannitol diuresis. Allow for marrow recovery before proceeding to Regimen B.

Regimen B: VCR - 2 mg/sqm (maximum 2 mg) iv; MTX - 7.5 g/sqm iv over 6 hours, beginning 30 minutes after VCR; CF - 15 mg/sqm iv q 3 hours for 24 hours, then q 6 hours for 48 hours, beginning 2 hours after termination of MTX infusion; ADR - 70 mg/sqm iv on day 4. Repeat cycle q 21 days until cumulative ADR dose is 560 mg/sqm; then continue MTX-CF alone for a total of 24 cycles.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

10.0008 PILOT STUDY OF ADJUVANT THERAPY WITH ADRIAMYCIN/CIS-PLATINUM FOR OSTEOGENIC SARCOMA

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PROTOCOL NUMBER(S) ARG-SAO-7804

OBJECTIVES:

I. Determine the disease-free interval and survival for patients treated with adriamycin (ADR)/cis-platinum (CACP).

II. Determine the toxicity and amount of drug that can be safely administered to these adjuvant patients.

PROTOCOL ENTRY CRITERIA: Patients with osteogenic sarcoma after radical ablation of the tumor. Patients under 20 years of age must have biopsy proven disease. Osteosarcoma may not be radiation induced, follow Paget's disease or be parosteal osteosarcoma. Patients must not have failed to respond to prior Chemotherapy which may not have been administered for more than 1 month. Patients must have adequate bone marrow, renal and hepatic function and have no history of chronic renal, liver or heart disease.

PROTOCOL OUTLINE: Nonrandomized study. Surgery plus 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Chest tomogram, CAT bone scan, IVP, arteriography, venography, lymphangiography, audiogram.

END POINTS: Disease-free interval, survival rate, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE: Surgery. Definitive amputation or radical ablation of tumor. Begin Chemotherapy 7 to 10 days postoperative or when wound healing is adequate. ADR - 30 mg/sqm iv on days 1 through 3. CACP - 50 mg/sqm with diuresis iv on days 28 and 29. Repeat course q 8 weeks for 6 courses. Then continue CACP alone q 4 weeks. Adjuvant therapy continues for 1 year or until progression or severe toxicity. Follow all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP, ADR - Not given.

DATE SUMMARIZED: 12/78

10.0009 MTX/CF/VCR CHEMOTHERAPY ALTERNATING WITH ADR/CTX PLUS RADIOTHERAPY VS CHEMOTHERAPY OR RADIOTHERAPY ALONE FOR OSTEOSARCOMA

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PROTOCOL NUMBER(S) EORTC-20781; EORTC-03; SIOP-03

OBJECTIVES:

I. Compare the effects of lung irradiation vs. systemic chemotherapy vs. a combination of radiation and chemotherapy after radical treatment of primary osteosarcoma of the limb with regard to metastases-free survival and morbidity of treatment.

II. Collect data on number, growth rate, and therapy induced growth retardation on lung metastases following different types of adjuvant therapy.

PROTOCOL ENTRY CRITERIA: Patients less than 30 years old with histologically diagnosed osteosarcoma of the limbs without known metastases. Patients must have had radical ablative surgery or radiotherapy of the primary tumor and no other prior treatment except a short series of radiotherapy before biopsy. Patient must not have juxtacortical osteosarcoma or other malignant tumors and must have adequate lung, kidney, and cardiac functions.

PROTOCOL OUTLINE: Randomized study. Separately randomize patients treated by surgery and those treated by radiotherapy.

Arm I: 3-Drug Combination Chemotherapy alternating with 2 Single-agent Chemotherapies. Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590; Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm II: Radiotherapy. Megavoltage x-rays or Cobalt-60 gamma rays to the thorax.

Arm III: 2-Drug Combination Chemotherapy plus Radiotherapy. MTX/CF/ADR as initially in Arm I, followed by radiotherapy, as in Arm II.

STRATIFICATION BY: Treatment of primary tumor: radiotherapy or surgery.

SPECIAL STUDY PARAMETERS: EKG; lung function tests; isotope scans, lung tomograms if indicated.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, disease-free interval, survival rate, number and growth rate of developing metastases.

CURRENT STATUS: About 300 patients will be entered; 120 patients on study as of August 1980.

DOSAGE SCHEDULE:

Enter all patients as soon as possible and no later than 4 weeks after ablative surgery or radiotherapy. Chemotherapy may be started simultaneously with radiotherapy, but monitor tolerance.

Arm I: VCR - 1.5 mg/sqm (maximum 2.0 mg) iv on days 1, 29, and 57 followed 6 hours later by MTX - 6000 mg/sqm iv in a 6-hour infusion followed 2 hours later with CF - 12 mg iv q 6 hours for 12 doses (or 15 im or po for 12 doses); ADR - 70 mg/sqm iv on days 15 and 43; CTX - 1200 mg/sqm iv on days 71 and 99; ADR, as above, on day 85; and VCR, MTX, and CF, as above, on day 113. Repeat course from day 71 to day 113 for 3 additional courses, with a 5-week maximal delay between courses. Enforced diuresis must be maintained at least until 48 hours after MTX infusion.

Arm II: Radiotherapy - 200 rad daily for a total dose of 2000 rad in 12 days in the anterior/posterior midplane of the lungs to the total contents of the thoracic cavity, including pleural sinuses and mediastinum.

Arm III: Chemotherapy. MTX and CF as in Arm I on days 1, 29, and 57; ADR, as in Arm I on days 15 and 43; followed on day 71 with lung irradiation as in Arm II. Maximum interval between chemotherapy and beginning of radiotherapy is 5 weeks.

Continue follow-up of patients as long as they live. Follow up all patients at least q 4 weeks in the first 6 months, q 6 weeks in the next 18 months, q 2 months in the 3rd year, q 3 months in the 4th year, and q 4 months in the fifth year.

Separately treat and document treatment of lung metastases. If feasible, perform pulmonary surgery within 3 to 6 weeks of discovery of metastases, and measure growth rates.

Dosage modifications for toxicity are given.

DOSAGES FORMS: Not given.

DATE SUMMARIZED: 05/79

10.0010 HIGH-DOSE MTX VS LOW-DOSE MTX CHEMOTHERAPY FOR ADVANCED OSTEOSARCOMA

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PROTOCOL NUMBER(S) EORTC-62782

OBJECTIVES:

I. Study the efficacy and toxicity of low- and high-dose MTX chemotherapy in metastatic osteogenic sarcoma, comparing the remission rate, duration of remission, and survival of the two treatment groups.

II. Ascertain how often metastatic disease that is unresponsive to low doses of MTX will subsequently respond to high doses.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed osteosarcoma, with measurable lung metastasis. Patients must be between the ages of 5 and 50 years, have a performance status (Karnofsky) under 50 and normal hematologic and renal function. Patients must have no overt psychosis, marked senility, second active tumor, serious concomitant disease, or brain metastases. Patients must have received no treatment with methotrexate within the 6 months prior to entry and no other chemotherapy within the 4 weeks prior to entry. Patients must have received no radiotherapy to disease areas being measured in this protocol.

PROTOCOL OUTLINE: Randomized study. Study randomized with respect to dose level. Patients who show progression on the low-dose arm cross overto the high-dose arm.

Arm I: Single-agent Chemotherapy. Low-dose Methotrexate, MTX, NSC-740.

Arm II: Single-agent Chemotherapy. High-dose MTX; Citrovorum Factor, CF, NSC-3590.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Chest and skeletal x-ray, lung tomography, isotopic scintigraphy.

END POINTS: Remission rate, duration of remission, survival.

CURRENT STATUS: 10 patients have been entered as of July 7, 1980. Up to 150 patients will be entered.

DOSAGE SCHEDULE:

Arm I: MTX - 80 mg/sqm iv on days 1, 8, and 15, then q 2 weeks. Patients with stable disease on day 57 cross over to Arm II. Patients with remission of disease continue treatment until progression.

Arm II: MTX - 7.5 g/sqm in a 6-hour iv infusion with adequate diuresis and alkalinization of the urine. Start CF - 15 mg/sqm iv 2 hours after the termination of MTX infusion. CF is continued po (same dose) q 6 hours for a total of 16 doses. CF dose may be modified according to the plasma MTX concentration. Course is given on days 1, 8, and 15, and then q 2 weeks. Treatment continues until progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

10.0011 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR ADVANCED OSTEOGENIC SARCOMA

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PROTOCOL NUMBER(S) EORTC-62794

OBJECTIVES:

I. Determine the rate of complete and partial responses as well as the duration of response in patients with metastatic osteogenic sarcoma treated with cis-platinum.

II. Determine the morbidity of cis-platinum in this group of patients.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed osteosarcoma and measurable lung metastases. Patients must be between the ages of 5 and 50 years, have a Karnofsky performance status of at least 50 percent, and have normal hematologic and renal function. Patients must have no overt psychosis, senility, or brain metastases or serious concomitant disease. Patients must have no previous therapy with cis-platinum and no previous radiotherapy to the lesions to be evaluated for response in this study. Patients must not receive any chemotherapy for at least the 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Hematologic function tests, tumor measurements, renal and hepatic function tests, chest x-ray, skeletal x-ray, audiogram.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: Initially 20 patients will be considered; then 5 more will be entered for each response observed, to a total of 40 patients. 11 patients have been entered as of July 1980.

DOSAGE SCHEDULE:

CACP - 100 mg/sqm iv 24-hour continuous infusion q 3 weeks. CACP is administered with prehydration, 12 g mannitol diuresis, and posthydration. If there is tumor regression after the 2nd course, treatment is continued until progression; if there is progression, patient goes off study. If there is stable disease, two additional courses are given. If no response is observed, patient goes off study. Responders continue treatment until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

10.0012 ADJUVANT PROPHYLACTIC COMBINATION CHEMOTHERAPY WITH VCR/MTX/CF/ADR OR VCR/MTX/CF FOR OCCULT LUNG METASTASES IN OSTEOSARCOMA

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PROTOCOL NUMBER(S) UICC-76052; UKM-MRC-WPBS-A

OBJECTIVES:

I. Evaluate the efficacies of two chemotherapeutic regimens (vincristine/methotrexate/citrovorum factor/adriamycin or vincristine/methotrexate/citrovorum factor) as prophylaxis for lung metastases following either surgery alone or radiotherapy with or without surgery for treatment of osteosarcoma.

PROTOCOL ENTRY CRITERIA: Patients with proven osteosarcoma without evidence of metastases in the lungs or elsewhere. Patients must have undergone primary amputation or radiotherapy followed 6 to 9 months later by amputation, if there is no evidence of metastases (Cade method). Patients with tumors unsuitable for primary amputation are treated by radiotherapy and randomized separately. Patients who have undergone tumor resection (not amputation) alone are ineligible.

PROTOCOL OUTLINE: Randomized study. Separately randomize 3 groups of patients: Group I (patients with primary amputations only), Group II (patients treated with radiotherapy, not less than 6000-7000 rads in 6-7 weeks, followed by amputation), and Group III (patients treated with radiotherapy alone). Enter Group I patients within 2 weeks of surgery and Group III patients concurrent with radiotherapy, provided hematologic status is adequate.

Arm I: 3-Drug Combination Chemotherapy alternating with Single-agent Chemotherapy. Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590, alternating with Adriamycin, ADR, NSC-123127.

Arm II: 3-Drug Combination Chemotherapy. VCR; MTX; CF.

STRATIFICATION BY: Participating institutions, prior surgery, prior radiotherapy, age: below 11 years vs. 11-20 years vs. 21-39 years.

SPECIAL STUDY PARAMETERS: Whole-lung tomography, skeletal survey, LFT.

END POINTS: Toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, appearance and progress of lung metastases, quality of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Alternate 3-Drug Therapy with ADR q 3 weeks for a total of 9 courses (54 weeks). VCR - 2 mg/sqm (maximum dose 2 mg) iv on days 1, 42, etc., followed 30 minutes later by MTX - 200 mg/sqm iv on day 1, 42, etc., followed 24 hours later by CF - 10 mg iv or im or po (after the 1st dose) repeated q 6 hours for 6 doses. ADR - 60 mg/sqm (maximum cummulative dose 540 mg/sqm) iv on days 21, 63, etc.

Arm II: Repeat course q 3 weeks for 18 courses (54 weeks). VCR followed by MTX followed by 6 doses of CV, as in Arm I.

Monitor hematological, liver, renal and cardiac functions in all patients, and follow up patients for life.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

10B. SOFT TISSUE SARCOMA

10.0013 PHASE II CHEMOTHERAPY WITH AMSA FOR MALIGNANT MESOTHELIOMA OF THE PLEURAL OR PERITONEAL CAVITY

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PROTOCOL NUMBER(S) EST-PA-380

OBJECTIVES:

I. Assess the effectiveness of m-AMSA in patients with nonresectable diffuse or localized malignant mesothelioma of the pleural or peritoneal cavity in terms of duration and quality of survival, response, and duration of response.

PROTOCOL ENTRY CRITERIA: Patients under 70 years of age with measurable or evaluable, nonresectable, histologically confirmed malignant mesothelioma of the pleural or peritoneal cavity. Nonirradiated disease must be present. Patients must have a performance status of 3 or better and adequate hematologic, hepatic, and renal function. Patients must not have active heart disease or have had surgery within 2 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Disease involvement: pleural involvement with or without peritoneal extension vs. peritoneal involvement only; participating institutions.

SPECIAL STUDY PARAMETERS: Chest x-ray; EKG; pulmonary functions; hematologic, hepatic, and renal function tests; tumor measurements; histology; bone and liver scans; tomograms.

END POINTS: Response/remission rate, duration of response, survival rate, length of survival.

CURRENT STATUS: Up to 30 patients will be entered.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv infusion over 60 minutes q 21 days, provided recovery from myelosuppression is complete. Dose is reduced to 90 mg/sqm for patients with prior radiotherapy and/or chemotherapy. Patients will continue treatment until disease progression or unmanageable toxicity, all patients receiving at least 2 courses of treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 08/80

10.0014 ADJUVANT CHEMOTHERAPY WITH ADRIAMYCIN FOR SOFT TISSUE SARCOMA

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PROTOCOL NUMBER(S) EST-2377

OBJECTIVES:

I. Determine the effect of adjuvant chemotherapy with adriamycin following primary therapy of soft tissue sarcomas in patients at high risk of recurrence.

PROTOCOL ENTRY CRITERIA: Patients between 16 and 75 years of age with recent surgical or surgical plus radiation treatment for soft tissue sarcomas of the following histological types (excluding lesions of hollow viscera, parenchymatous organs, and within the dura): All stages except Stage IVB of synovial, alveolar soft parts, not designated, and rhabdomyosarcomas; all Stages except Stages I, IIA, and IVB of fibrosarcoma, malignant fibrohistiocytoma, liposarcoma, angiosarcoma, leiomyosarcoma, malignant schwannoma, malignant mesenchyoma, extra-skeletal osteosarcoma, and extra-skeletal chondrosarcoma. Patients must have adequate hematologic and hepatic function, normal renal function, and a report of clear margins in their postoperative pathology report if primary treatment was surgery alone. Patients must be free of clinically detectable disease, postoperative complications and acute side effects of radiotherapy, previous therapy with adriamycin, radiation to involved area, arrhythmia or myocardial damage, and previous cancer (except basal cell or squamous cell of the skin).

PROTOCOL OUTLINE: Randomized study. Enter patients within 6 weeks after Surgery if no Radiotherapy was given and within 12 weeks if Radiotherapy was given.

Arm I: No Chemotherapy.

Arm II: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions; cell type (see Patient Entry Criteria); primary treatment: radical surgery vs. conservative surgery plus radiotherapy; Stage: I or II vs. III or IV.

SPECIAL STUDY PARAMETERS: Whole lung tomography, metastatic survey, bone and liver scan, SMA-12.

END POINTS: Survival time, duration of response.

CURRENT STATUS: About 50 patients will be entered per year.

DOSAGE SCHEDULE:

Arm I: No therapy.

Arm II: ADR - 70 mg/sqm iv q 3 weeks for 7 courses. Follow patients until disease recurrence and then until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 10/78

10.0015 PHASE I-II PILOT CHEMOTHERAPY WITH ADRIAMYCIN/DTIC FOR SOFT TISSUE SARCOMAS

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7765

OBJECTIVES:

I. Determine the effectiveness and tolerance of adriamycin and single-dose DTIC in patients with metastatic sarcomas who have failed on higher priority treatment protocols.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven soft tissue sarcomas with measurable metastases, who may have received appropriate surgery and are refractory to prior therapy with cyclophosphamide and/or actinomycin-D. Patients must have a life expectancy of at least 6 weeks, must have recovered from and been off all prior chemotherapy or radiotherapy for 3 weeks, must have an absolute granulocyte count of at least 2000 and a platelet count of at least 100,000, and must have adequate liver and renal functions. Patients classified as those having inadequate bone marrow reserves are either above 60 years of age, and/or have had extensive radiotherapy involving active bone marrow portions of the body, and/or have had extensive prior chemotherapy defined as permanent hypoplasia of the bone marrow, and/or have a history of intolerance to myelosuppressive chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; DTIC, NSC-45388.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Creatinine, phosphokinase, liver and renal function tests.

END POINTS: Toxicity/morbidity of treatment, objective tumor response, response/remission rate, response duration, survival duration.

CURRENT STATUS: About 25 patients will be entered.

DOSAGE SCHEDULE:

ADR - 50 mg/sqm iv on day 1 followed by DTIC - 750 mg/sqm iv on day 1. For patients with inadequate bone marrow reserves, reduce ADR to 40 mg/sqm and DTIC to 500 mg/sqm. Repeat course q 21 days. When a total cumulative ADR dose of 500 mg/sqm has been given, continue DTIC therapy alone. Discontinue therapy for unacceptable toxicity, for increasing disease after 2 courses or after 2 years in complete remission.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg ampules; DTIC - 100 and 200 mg ampules.

DATE SUMMARIZED: 06/78

PATIENT ACCRUAL: 00120179

10.0016 COMBINATION CHEMOTHERAPY WITH ADR/CTX PLUS WHOLE BODY HYPERTHERMIA FOR METASTATIC SOFT TISSUE SARCOMA

Van Echo, D. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7906

OBJECTIVES:

I. Assess the toxicities of the combination of cyclophosphamide and adriamycin when given concurrently with hyperthermia in patients with advanced soft tissue sarcoma.

II. Determine the therapeutic efficacy of hyperthermia combined with adriamycin/cyclophosphamide in the treatment of these patients.

III. Measure the clinical pharmacokinetics of cyclophosphamide and adriamycin during hyperthermia.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven soft tissue sarcoma not amenable to surgery. Patients must have measurable disease and may not have had prior chemotherapy or radiotherapy to present sites of disease. There must be no evidence of coronary artery disease, and pulmonary function must be reasonable. Liver function and bone marrow reserves must be adequate. Patients must be ambulatory and under the age of 65 years.

PROTOCOL OUTLINE: Nonrandomized study. Enter all patients to Regimen A for the purpose of establishing pharmacokinetic controls. After at least 1 course of treatment of Regimen A, enter all patients to Regimen B.

Regimen A: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Regimen B: 2-Drug Combination Chemotherapy plus Whole-Body Hyperthermia. ADR; CTX.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Tumor measurements, chest x-rays, hemogram, SMA-12, creatinine, appropriate scans and x-rays as dictated clinically.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: ADR - 45 mg/sqm iv push over 10 minutes on day 1, total maximum cumulative dose not to exceed 450 mg/sqm; CTX - 1 g/sqm in 1-hour iv infusion beginning 6 hours after ADR. May be repeated at 28 days. Give at least 1 course before proceeding with Regimen B.

Regimen B: Hyperthermia - 2 hours at 41.8 degrees Centigrade. ADR and CTX as in Regimen A, with ADR beginning when maximum temperature is reached. Give at least 2 courses before declaring failure. All patients with a response will be continued on treatment for 1 year or until relapse. Development of life-threatening toxicity will be cause for termination of study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

10.0017 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE (DHAD) FOR METASTATIC SOFT TISSUE SARCOMA

Van Echo, D. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-8016

OBJECTIVES:

I. Determine response rate and remission duration in previously treated patients with advanced soft tissue sarcoma treated with dihydroxyanthracenedione (DHAD) used in a single dose daily for 3 days every 3 weeks.

II. Define the qualitative and quantitative toxicities of DHAD administered in a Phase II study.

PROTOCOL ENTRY CRITERIA: Patients with histologic proof of soft tissue sarcoma that is objectively measurable. Patients must have failed conventional chemotherapy, must not be eligible for any other BCRP protocol of higher priority, and must have a minimum life expectancy of six weeks. Patients must receive no chemotherapy or radiotherapy within 4 weeks (8 weeks for nitrosoureas) of entry. Solid tumor patients should have adequate bone marrow, hepatic, and renal function. Patients may have prior anthracycline exposure.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: BUN, creatinine, liver function tests, scans or x-rays as needed.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, response/remission rate.

CURRENT STATUS: 14-25 patients will be entered.

DOSAGE SCHEDULE:

DHAD - initial dose of 4 mg/sqm/day iv push through a rapidly running infusion of DSW over 10 minutes for 3 days q 3 weeks, provided there is recovery from toxicity. Subsequently, if there are no side effects, drug dose is increased by 1 mg/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 2.5 and 5 mg ampules.

DATE SUMMARIZED: 10/80

10.0018 CHEMOTHERAPY WITH CTX PLUS CONTINUOUS INFUSION OF ADR AND DTIC FOR METASTATIC OR UNRESECTABLE SOFT TISSUE SARCOMA

Benjamin, R. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-379; MDA-DT-7968

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with single dose cyclophosphamide and 4-day continuous infusion of adriamycin and DTIC in the treatment of patients with metastatic or inoperable locally advanced soft tissue sarcomas.

II. Prolong remission by continuing adriamycin chemotherapy for 9-18 months or until cardiac toxicity manifested by Grade II endomyocardial biopsy changes or clinical congestive heart failure occurs.

III. Maximize tumor reduction by surgical excision of accessible lesions in responding patients.

IV. Maximize tumor reduction by intraarterial administration of adriamycin and DTIC in patients with bulky regional tumors.

PROTOCOL ENTRY CRITERIA: Patients with metastatic or unresectable soft tissue sarcomas who have not had prior chemotherapy and who have measurable lesions. Patients must have a life expectancy of at least 12 weeks and they must be off prior treatment, including radiotherapy, for at least 4 weeks prior to entry. Bone marrow function must be adequate, and patients must have recovered from the toxic effects of prior treatment.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; DTIC, NSC-45388; Cyclophosphamide, CTX, NSC-26271. (Patients with rhabdomyosarcoma, Ewing's sarcoma, or undifferentiated sarcoma also receive Vincristine, VCR, NSC-67574.)

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, echocardiogram, cardiac scan, endomyocardial biopsy, cardiac ejection fraction.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: About 50 evaluable patients will be entered.

DOSAGE SCHEDULE:

A central venous silastic catheter will be inserted prior to the first course of chemotherapy and maintained throughout the treatment program.

CTX - 600 mg/sqm iv infusion on day 1; ADR - 60 mg/sqm continuous iv infusion over 96 hours; DTIC - 1 g/sqm by continuous iv infusion over 96 hours. Cycles repeated at 3-week intervals (4 weeks if granulocytes are below 1500 and platelets below 100,000) for 18 months or relapse or until cardiac toxicity is manifested. For patients with rhabdomyosarcoma, Ewing's sarcoma, or undifferentiated sarcoma, Vincristine should be added to the regimen - 2 mg/week iv for 6 weeks, thereafter on day 1 of each cycle. In the absence of infection, severe stomatitis, or granulocytopenia, doses of ADR and CTX will be increased to 75 mg/sqm and 750 mg/sqm, respectively, for the second course and to 90 mg/sqm and 900 mg/sqm for the third course.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/80

10.0019 VAC (VCR/CTX/ADR) COMBINATION CHEMOTHERAPY WITH & WITHOUT MIXED BACTERIAL VACCINE IMMUNOTHERAPY AS ADJUVANT TREATMENT OF SOFT TISSUE SARCOMA

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PROTOCOL NUMBER(S) MSKCC-7962

OBJECTIVES:

I. Decrease the recurrence rate in patients who have had soft tissue sarcomas resected by combination chemotherapy with vincristine, adriamycin, and cyclophosphamide with and without immunotherapy with mixed bacterial vaccine (MBV).

II. Test the efficacy of MBV immunotherapy in increasing the disease-free interval in these patients.

PROTOCOL ENTRY CRITERIA: Adults who have had surgical resection of soft tissue sarcomas and who, because of grade of malignancy, poor histology, or bulky disease preoperatively, are considered to be at high risk for recurrence. Patients with low grade liposarcomas, fibrosarcomas, or leiomyosarcomas will be excluded. Patients must have normal liver function and adequate hematological reserves and must not have had significant prior anthracycline therapy (not more than 100 mg/sqm).

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. VAC: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Arm II: 3-Drug Combination Chemotherapy plus Immunotherapy. VAC plus Mixed Bacterial Vaccine (MBV).

STRATIFICATION BY: Disease status (Group I, II, or III).

SPECIAL STUDY PARAMETERS: In-vitro testing for immunity and skin tests for delayed hypersensitivity in selected patients.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, survival rate.

CURRENT STATUS: About 100 patients will be entered during 3 years.

DOSAGE SCHEDULE:

Arm I: VAC: VCR - 1 mg/sqm iv (maximum 2 mg); ADR - 50 mg/sqm iv; CTX - 700 mg/sqm iv. Repeat at 4-week intervals for 9 cycles (total ADR 450 mg/sqm).

Arm II: VAC as in Arm II plus 0.1 ml of 10 to the minus 2 MBV, sc, with the dose increased daily by one-half log; highest tolerated dose will be continued at 2-week intervals over a period of 72 weeks.

Follow patients at 4-week intervals for 18 months and at increasing intervals for a minimum of 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 06/80

10.0020 CHEMOTHERAPY WITH ADRIAMYCIN PLUS RADIOTHERAPY FOLLOWED BY 5-AZACYTIDINE FOR MALIGNANT MESOTHELIOMA

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PROTOCOL NUMBER(S) MTS-2; MTS-76/73-NPD-CR

OBJECTIVES:

I. Assess the efficacy of adriamycin (ADR) for mesothelioma.

II. Assess the effect of combining local radiotherapy with ADR for mesothelioma in order to determine the radiosensitizing effect of ADR.

III. Assess the efficacy of 5-azacytidine for mesothelioma.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven, malignant mesothelioma of the pleura or peritoneum (diffuse type). Patients must be free of clinically significant metastatic disease, must not have had prior radiotherapy and/or chemotherapy with adriamycin or 5-azacytidine; however, patients who have undergone prior palliative surgery or prior curative surgery with subsequent relapse are eligible. Patients must have normal blood count and hepatic function, and creatinine must be less than 1.4 mg%.

PROTOCOL OUTLINE: Nonrandomized study.

Sequential 2-Drug Combination Chemotherapy plus Radiotherapy. Adriamycin, ADR, NSC-123127; Azacytidine, AZC, NSC-102816.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: SMA-6 and 12, stool guaiac, liver, bone, and gallium scan, alphafetoprotein, CEA, pulmonary function, cytology spectrum, pleural fluid, upper GI series, barium enema, skin tests for recall antigens, in vitro lymphocyte reactions.

END POINTS: Objective tumor response, response/remission rate, disease progression, toxicity/morbidity of treatment, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: ADR - 30 mg/sqm/day (total cumulative dose - 550 mg/sqm) iv slow infusion on days 1, 2 and 3. Repeat course q 3 weeks and concurrently with the second course give 2000 to 3000 rad to chest and abdomen, if cbc is normal. If there is response to ADR, delay Radiotherapy until relapse or progression. Continue ADR therapy q 3 weeks if wbc are above 3000, platelets above 100,000. Three weeks after completion of ADR therapy or at any evidence of relapse or recurrence and when all ADR toxicity has disappeared (Patients must have normal cbc and creatinine less than 1.4 mg percent before each injection), give AZC - 100 mg/sqm iv by rapid injection twice a week for 1 week. If well tolerated, give 150 mg/sqm twice a week thereafter. Continue treatment until patient demonstrates disease progression or drug intolerance.

Addendum (no date given):

Give patients who are ineligible for above protocol because of widespread disease or abdominal mesothelioma ADR - 25 mg/sqm/day iv into tubing of running infusion on days 1, 2 and 3 q 4 weeks; AZC - 120 mg/sqm/day iv continuous 24-hour infusion on days 1 through 5 q 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

10.0021 RADICAL SURGERY AND CHEMOTHERAPY VS CONSERVATIVE SURGERY AND RADIOTHERAPY WITH/WITHOUT CHEMOTHERAPY FOR SOFT TISSUE SARCOMA OF THE EXTREMITIES

Rosenberg, S. A., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America

PROTOCOL NUMBER(S) NCI-76-C-191; NCI-SB-S4

OBJECTIVES:

I. Evaluate the relative efficacy of radical surgery compared to conservative surgery plus radiotherapy in the management of nonmetastatic sarcoma of the extremities.

II. Assess the value of chemotherapy with cyclophosphamide/adriamycin followed by high-dose methotrexate with leukovorin rescue as an adjunct to surgery in patients with soft tissue sarcoma of the extremities.

PROTOCOL ENTRY CRITERIA: Patients under the age of 65 with biopsy-proven liposarcoma, rhabdomyosarcoma, synoviosarcoma, unclassified sarcoma, fibrosarcoma, neurofibrosarcoma, leiomyosarcoma, malignant mesenchymoma, angiosarcoma, or malignant fibrous histiocytoma. The soft tissue sarcoma must be on an extremity, lesions must be at least 5 cm in diameter, and there must be no clinical evidence of metastatic disease. The tumor must be considered to be completely removable by radical surgery. Patients may have undergone local excision within 6 months of entry and may have had local recurrence but not metastasis following that local excision. There must have been no chemotherapy, radiotherapy, or radical excision prior to entry. Patients with rhabdomyosarcoma must be 21 years of age or older. Bone marrow function must be adequate and there must be no serious infection, bleeding disorder, or concomitant serious disease. There must be no history of any other malignant disease except basal cell carcinoma.

PROTOCOL OUTLINE: Randomized study. Randomize patients initially to Arms I and II; Arm I patients subsequently enter Arm III, and Arm II patients enter Arm IV. Concomitant with treatment in Arm IV, patients are randomized to Arms V and VI.

Arm I: Radical Surgery.

Arm II: Conservative Surgery.

Arm III: 2-Drug Combination Chemotherapy followed by Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; followed by Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

Arm IV: Radiotherapy.

Arm V: 2-Drug Combination Chemotherapy followed by Single-agent Chemotherapy. ADR; CTX; followed by MTX; CF.

Arm VI: No further treatment.

STRATIFICATION BY: Tumor type (rhabdomyosarcoma, fibrosarcoma, liposarcoma, neurofibrosarcoma, leiomyosarcoma, malignant mesenchymoma, and malignant histiosarcoma vs. synoviosarcoma, unclassified sarcoma, and angiosarcoma); histologic grade (I and II vs. III); interval since diagnosis or local excision elsewhere (2 months or less vs. more than 2 months); local recurrence following local excision elsewhere (yes vs. no); location of lesion (extension to proximal half of extremity vs. no extension to that area).

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, bone marrow aspiration, EKG, creatinine clearance, chest x-ray, chest tomograms, immunologic studies, blood chemistries, bone scan, abdominal EMI and ultrasound as indicated.

END POINTS: Response/remission rate, duration of response, disease-free interval, survival, toxicity/morbidity of treatment.

DOSAGE SCHEDULE:

Arm I: Amputation of the involved extremity at or including the joint proximal to the lesion.

Arm II: En-bloc resection of the tumor with an attempt to obtain negative microscopic margins but with retention of a useful extremity as a prime consideration.

Arm III: ADR - 50 mg/sqm slow iv push on day 1; CTX - 500 mg/sqm iv over 15-20 minutes on day 1, with adequate hydration before and after administration. Repeat course q 28 days. Discontinue ADR/CTX after total cumulative dose of ADR reaches 550 mg/sqm and give MTX and CF as follows: MTX - 50 mg/kg iv over 6 hours; CF - 15 mg/sqm iv 2 hours after completion of MTX infusion and repeated q 6 hours for a total of 8 doses. Patients should be well hydrated and urine alkalinized. Repeat q 28 days for a total of 6 courses.

Arm IV: 5,000 rads over 5-6 weeks to the entire involved portion of the extremity between the joints proximal and distal to the tumor followed by tumor-bed irradiation using a shrinking field technique for a total of 6000-7000 rads. Treatment will begin as soon as the wound is healed.

Arm V: Chemotherapy as in Arm III given concomitantly with Radiotherapy in Arm IV.

Arm VI: No treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

10.0022 SURGERY PLUS RADIOTHERAPY PLUS ADR/CTX FOLLOWED BY MTX VS SURGERY PLUS RADIOTHERAPY ALONE FOR SOFT TISSUE SARCOMA OF THE HEAD, NECK, OR TRUNK

Rosenberg, S. A., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America

PROTOCOL NUMBER(S) NCI-76-C-192; NCI-SB-S5

OBJECTIVES:

I. Assess the value of chemotherapy with adriamycin/cyclophosphamide followed by methotrexate/citrovorum factor as an adjunct to surgery in patients with soft tissue sarcoma of the head, neck, or trunk.

PROTOCOL ENTRY CRITERIA: Patients under the age of 65 with biopsy-proven liposarcoma, rhabdomyosarcoma, leiomyosarcoma, synoviosarcoma, unclassifiable sarcoma, fibrosarcoma, neurofibrosarcoma, malignant mesenchymoma, angiosarcoma, or malignant fibrous histiocytoma located in the head, neck, or trunk and without metastasis locally or to a distant site. Patients may have undergone local excision within 6 months of entry and may have local recurrence but not metastasis following that local excision. There may have been no prior chemotherapy or radiotherapy. Patients with rhabdomyosarcoma must be 21 years of age or older. Bone marrow function must be adequate and there must be no serious infection, bleeding disorder, or concomitant serious disease. There must be no history of any other malignant disease except basal cell carcinoma.

PROTOCOL OUTLINE: Enter patients to Regimens A and B, then randomize to Arms I and II.

Regimen A: Surgery.

Regimen B: Local Radiotherapy.

Arm I: 2-Drug Combination Chemotherapy followed by Single-agent Chemotherapy plus Leucovorin Rescue. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; followed by Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

Arm II: No further treatment.

STRATIFICATION BY: Tumor type (rhabdomyosarcoma, fibrosarcoma, liposarcoma, neurofibrosarcoma, leiomyosarcoma, malignant mesenchymoma, and malignant histiosarcoma vs. synoviosarcoma, unclassifiable sarcoma, and angiosarcoma), histologic grade (I and II vs. III), interval since diagnosis or local excision elsewhere (2 months or less vs. more than 2 months), local recurrence following local excision elsewhere (yes vs. no), tumor site (extension into the head and neck vs. trunk lesions), surgical margins (microscopically positive vs. negative).

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, bone marrow aspiration, EKG, creatinine clearance, chest x-ray, chest tomograms, immunologic studies, blood chemistries, bone scan, and abdominal EMI and ultrasound as indicated.

END POINTS: Response/remission rate, duration of response, disease-free interval, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Conservative excision removing as much tumor as is consistent with reasonable morbidity.

Regimen B: Beginning when wound has healed. 5000 rads over about 5 weeks, when possible using a shrinking-field technique to deliver a total of 6000-7000 rads to the tumor bed.

Arm I: Concomitant with Regimen B. ADR - 50 mg/sqm slow iv push infusion on day 1; CTX - 500 mg/sqm iv over 15-20 minutes on day 1, with adequate hydration before and after administration. Repeat course q 28 days to a total cumulative ADR dose of 550 mg/sqm, after which replace ADR and CTX with MTX and CF: MTX - 50 mg/kg iv over 6 hours; CF - 15 mg/sqm iv 2 hours after MTX infusion and repeated q 6 hours for a total of 8 doses. Patients should be well hydrated and urine alkalinized. Repeat q 28 days for a total of 6 courses.

Arm II: No further treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

10.0023 EVALUATION OF CHEMOTHERAPY WITH ADR/CTX AND MTX AS ADJUVANT THERAPY IN PATIENTS RECEIVING RADIOTHERAPY FOR SOFT TISSUE SARCOMA

Rosenberg, S. A., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America

PROTOCOL NUMBER(S) NCI-78-C-182; NCI-SB-S6

OBJECTIVES:

I. Evaluate the efficacy of adjuvant chemotherapy with adriamycin/cyclophosphamide followed by high-dose methotrexate and leukovorin rescue in adults receiving primary radiotherapy for soft tissue sarcomas of the extremities, head, neck, and trunk.

PROTOCOL ENTRY CRITERIA: Adult patients with biopsy-proven liposarcoma, rhabdomyosarcoma, synoviosarcoma, unclassifiable sarcoma, fibrosarcoma, neurofibrosarcoma, leiomyosarcoma, malignant mesenchymoma, angiosarcoma, or malignant fibrous histiocytoma located on an extremity or the head, neck, or trunk and with no evidence of metastasis. Patients must be ineligible for surgery by reason of tumor location or refusal to accept surgical options. Patients may be no older than 65 years and may have received no prior chemotherapy or radiotherapy for their sarcoma. Patients may have local recurrence without metastases after prior local excision within 6 months of entry. Bone marrow function must be adequate. Lesions must be at least 5 cm in diameter. There may be no prior malignancy except basal cell carcinoma, nor may there be any serious concurrent medical problem. Patients with rhabdomyosarcoma must be at least 21 years old.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy.

Arm II: Radiotherapy plus 2-Drug Combination Chemotherapy followed by Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; followed by Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

STRATIFICATION BY: Histologic grade (Grade I-II vs. Grade III), local recurrence following local excision prior to coming to NIH vs. no local recurrence.

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, bone marrow aspiration, EKG, creatinine clearance, chest x-ray, chest tomograms, immunologic studies, blood chemistries, bone scan, abdominal EMI and ultrasound as indicated.

END POINTS: Response/remission rate, duration of response, disease-free interval, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: 5000 rads over 5-6 weeks to the entire involved area, followed by tumor bed irradiation using a shrinking field technique, for a total of 6000-7000 rads.

Arm II: Radiotherapy as in Arm I. ADR - 50 mg/sqm slow iv push infusion on day 1; CTX - 500 mg/sqm iv over 15-20 minutes on day 1, with adequate hydration before and after administration. Repeat course q 28 days. Discontinue ADR/CTX after total cumulative dose of ADR reaches 550 mg/sqm and begin MTX/CF as follows: MTX - 50 mg/kg iv over 6 hours; CF - 15 mg/sqm iv 2 hours after completion of MTX infusion and repeated q 6 hours for a total of 8 doses. Patients should be well hydrated and urine alkalinized. Repeat q 28 days for a total of 6 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

10.0024 EVALUATION OF INTRAOPERATIVE RADIOTHERAPY & ADJUVANT CHEMOTHERAPY WITH CAM (CTX/ADR/MTX) FOR SOFT TISSUE RETROPERITONEAL SARCOMA

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PROTOCOL NUMBER(S) NCI-80-C-45; NCI-SB-S7

OBJECTIVES:

I. Evaluate the efficacy of intraoperative electron radiotherapy combined with low-dose postoperative external beam radiotherapy vs. postoperative conventional external beam radiotherapy for the local control of soft tissue sarcoma.

II. Evaluate toxicity and patient tolerance of both intraoperative radiotherapy with low-dose external beam postoperative radiation and postoperative conventional external beam radiotherapy.

III. Evaluate the efficacy in prolonging disease-free interval in retroperitoneal sarcoma by adjunctive chemotherapy with adriamycin/cyclophosphamide/methotrexate.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven soft tissue sarcomas of one of the following types: liposarcoma, rhabdomyosarcoma, synoviosarcoma, unclassifiable sarcoma, fibrosarcoma, neurofibrosarcoma, leiomyosarcoma, malignant mesenchymoma, angiosarcoma, malignant fibrous histiocytoma. There must be no clinical evidence of regional or distant metastases. Patients may present with local recurrence following local excision if all other requirements are met. There may be no prior chemotherapy or radiotherapy for the sarcoma. Bone marrow function must be adequate, and patients must be between the ages of 10 and 65 years, with 21 years the lower age limit for rhabdomyosarcoma patients.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I and II. Randomize patients from Arm I to Arms III and IV and those from Arm II to Arms IV and V.

Arm I: Surgery plus Conventional Postoperative External Beam Photon Radiotherapy.

Arm II: Surgery plus Intraoperative 6-11 MeV Electron Radiotherapy with Radiosensitization plus Postoperative Low-Dose External Beam Radiotherapy. Misonidazole, MNI, NSC-261037.

Arm III: 3-Drug Combination Chemotherapy plus Leucovorin Rescue. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590.

Arm IV: No further treatment.

Arm V: 3-Drug Combination Chemotherapy plus Leucovorin Rescue. ADR; CTX; MTX-CF.

STRATIFICATION BY: Tumor type (rhabdomyosarcoma, fibrosarcoma, liposarcoma, neurofibrosarcoma, leiomyosarcoma, malignant mesenchymoma vs. synoviosarcoma, unclassifiable sarcoma, angiosarcoma), histologic grade (relatively undifferentiated vs. relatively well differentiated), interval between diagnosis or prior excisional surgery and entry on study (2 months or less vs. more than 2 months), local recurrence following prior excision (yes vs. no).

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, bone marrow aspirate, EKG, creatinine clearance, chest x-ray, chest tomograms.

END POINTS: Response/remission rate, recurrence rate, pattern of recurrence, disease-free interval, toxicity/morbidity of treatment.

CURRENT STATUS: 26 patients will be required for each radiotherapy arm, accrual estimated to take 5 years. 36 patients will be required in each chemotherapy arm.

DOSAGE SCHEDULE:

Arm I: Surgical excision to remove as much tumor as is possible consistent with a reasonable morbidity. Radiotherapy - 5000 rads over 5 weeks, when possible using a shrinking field technique to deliver up to a total of 7000 rads to the tumor bed. Treatment to begin as soon as wound has healed.

Arm II: Surgery as in Arm I. Radiotherapy - 2000 rads over 5 minutes delivered intraoperatively 15 minutes after administration of MNI - 3.5 g/sqm iv over 5 minutes; 4500 rads over 4-5 weeks to the area thought to be at risk for tumor recurrence, beginning as soon as the surgical wound has healed.

Arm III: ADR - 50 mg/sqm slow iv push on day 1; CTX - 500 mg/sqm iv over 15-20 minutes on day 1; MTX - 50 mg/kg iv over 6 hours; CF - 15 mg/sqm iv q 6 hours for a total of 8 doses beginning 2 hours after completion of MTX. Begin Chemotherapy concomitantly with postoperative Radiotherapy and repeat cycles q 28 days. Escalate MTX by 50 mg/kg with each successive cycle to a maximum of 250 mg/kg. Discontinue ADR and CTX when total cumulative dose of ADR reaches 550 mg/sqm, and continue MTX-CF for 6 treatment cycles.

Arm IV: Observe.

Arm V: Treatment as in Arm III.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 500 mg ampules.

DATE SUMMARIZED: 08/80

10.0025 PHASE III CHEMOTHERAPY WITH ADRIAMYCIN FOR SOFT TISSUE SARCOMA STAGES IIIB THROUGH IVA

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PROTOCOL NUMBER(S) SFCC-78060

OBJECTIVES:

I. Evaluate the efficacy of adjuvant adriamycin compared to standard treatment of patients with Stage IIB, III and IVA soft tissue sarcoma.

PROTOCOL ENTRY CRITERIA: Patients with primary or recurrent soft tissue sarcoma, Stages IIB, IIIA, IIIB, IIIC, or IVA (Grade 2 or 3) at any anatomical site, including the following cell types: alveolar soft part sarcoma, angiosarcoma, fibrosarcoma, leiomyosarcoma, liposarcoma, malignant fibrohistiocytoma, malignant mesenchymoma, malignant schwannoma, rhabdomyosarcoma (excluding embryonal), sarcoma - type not designated. Patients must not have had prior chemotherapy or radiation therapy for this disease, and they must have adequate hematologic and cardiac status.

PROTOCOL OUTLINE: Randomized study. Randomize patients receiving surgery as primary therapy to Arms I or II, and patients receiving radiation as primary therapy to Arms III or IV. Randomize patients within 2 weeks of primary therapy.

Arm I: Postsurgical Single-agent Chemotherapy prior to and following Radiotherapy. Adriamycin, ADR, NSC-123127, plus Radiotherapy, type not specified.

Arm II: Radiotherapy alone.

Arm III: Postradiotherapeutic Single-agent Chemotherapy prior to and following Surgery. ADR.

Arm IV: Surgery alone.

STRATIFICATION BY: Participating institutions: MGH vs. SFCI; disease stage: IIB vs. IIIA through IVA; primary therapy: radiotherapy vs. surgery with or without residual disease.

SPECIAL STUDY PARAMETERS: Whole lung tomography, other radiographic studies as indicated, liver function tests.

END POINTS: Time to recurrence, site of recurrence, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: 120 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Begin all therapy within 2 weeks of primary treatment.

Arm I: ADR - 90 mg/sqm (route not stated) q 21 days for 2 courses before radiotherapy and for 3 courses following radiotherapy.

Radiotherapy: 6250 to 6750 rad given over a period of 6.5 to 7 weeks to the tumor bed and including the surgical scar, drainage tube site and all tissues involved in the surgical procedure. Reduce field size after 5500 to 6000 rad and again after 6250 to 6750 rad.

Arm II: Radiotherapy alone, as in Arm I.

Arm III: ADR - 2 courses as in Arm I, prior to resection of residual disease and 3 courses following, beginning within 2 weeks of surgery.

Arm IV: Surgery alone, within 6 weeks of primary radiotherapy.

The total cumulative dose of ADR given in Arms I and IV is 450 mg/sqm.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/79

10.0026 CHEMOTHERAPY WITH CYVADIC (CTX/VCR/ADR/DTIC) VS ADR/DTIC/CACP FOR ADVANCED SOFT TISSUE SARCOMAS

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PROTOCOL NUMBER(S) ARG-LACRIP-7

OBJECTIVES: This protocol is being done in cooperation with Georgetown University.

I. Compare the activity of CY-VA-DIC: cyclophosphamide (CTX)/vincristine (VCR)/adriamycin (ADR)/DTIC vs. ADR/DTIC/cis-platinum (CACP) for advanced soft tissue sarcomas.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven soft tissue sarcoma, including fibrous mesothelioma, not amenable to cure by surgery or Radiotherapy. Patients must have completed previous Chemotherapy more than 3 months ago and may not have had prior therapy with ADR or CACP. Patients must have adequate renal function and cardiac condition.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. CY-VA-DIC: Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; DTIC, NSC-45388. Actinomycin-D, ACT-D, NSC-3053, replaces ADR after maximum dose.

Arm II: 3-Drug Combination Chemotherapy. ADR; DTIC; cis-Platinum, CACP, NSC-119875. ACT-D replaces ADR after maximum dose.

STRATIFICATION BY: Extent of disease, previous therapy, histologic diagnosis and subclass.

SPECIAL STUDY PARAMETERS: Hepatic, renal, bone marrow function; neurologic status; protein electrophoresis; audiogram.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, response rate.

CURRENT STATUS: 20 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: CTX - 600 mg/sqm iv on day 1; VCR - 1.5 mg/sqm (maximum dose 2 mg) iv on day 1; ADR - 60 mg/sqm on day 1 (maximum cumulative dose 450-500 mg/sqm after which replace with ACT-D - 0.3 mg/sqm iv on days 1 through 3); DTIC - 250 mg/sqm iv on days 1 through 5. Repeat q 3 to 4 weeks as patient toxicity allows.

Arm II: CACP - 80 mg/sqm iv on day 1 (with hydration and mannitol diuresis); ADR - 60 mg/sqm iv given 4 hours before CACP on day 1 (maximum cumulative dose 450-500 mg/sqm after which replace with ACT-D -0.3 mg/sqm iv on days 15 through 17; DTIC - 250 mg/sqm iv on days 2 through 6. Repeat q 3 to 4 weeks for 6 to 8 courses.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/78

10.0027 COMBINATION CHEMOTHERAPY WITH ADR/DTIC/CTX/VCR FOR METASTATIC SOFT TISSUE SARCOMA

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PROTOCOL NUMBER(S) EORTC-62761; ITA-MIL-7603

OBJECTIVES:

I. Investigate the remission rate and duration of remission and survival of two schedules, a single-dose schedule and a cyclic schedule, of 4-drug treatment with adriamycin, DTIC, cyclophosphamide, and vincristine in soft tissue sarcoma.

PROTOCOL ENTRY CRITERIA: Patients, between 14 and 75 years of age, with confirmed and measurable residual or metastatic soft tissue sarcoma. Patients must not have an active second tumor or a serious concomitant disease, or have undergone prior chemotherapy with adriamycin, DTIC, vincristine or cyclophosphamide.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; DTIC, NSC-45388; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574.

Arm II: 4-Drug Cyclical Chemotherapy. ADR plus DTIC; CTX plus VCR.

STRATIFICATION BY: Cell type; age -between 15 and 59 years or between 60 and 75 years.

SPECIAL STUDY PARAMETERS: Skeletal X-ray survey; liver scan; skull, spine and pelvis scan.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response, duration of remission, survival rate, progression/relapse.

CURRENT STATUS: About 300 patients will be entered.

DOSAGE SCHEDULE:

Arm I: For patients between 15 and 59 years of age: ADR - 50 mg/sqm, iv on day 1; DTIC - 250 mg/sqm/day, iv, for days 1 through 5; CTX - 500 mg/sqm, iv, on day 1; VCR - 1.5 mg/sqm (maximum 2 mg), iv, on day 1. Repeat course q 3 weeks. For patients between 60 and 75 years of age: ADR - 35 mg/sqm, iv, on day 1; DTIC - 170 mg/sqm/day, iv, for days 1 through 5; CTX - 330 mg/sqm, iv on day 1; VCR - 1 mg/sqm, iv, on day 1. Repeat course q 3 weeks.

Arm II: For patients between 15 and 59 years of age; ADR - 50 mg/sqm, iv, on day 1, plus DTIC - 250 mg/sqm/day, iv, for days 1 through 5. CTX - 1200 mg/sqm, iv, on day 1, plus VCR - 1.5 mg/sqm (maximum 2 mg), iv, on day 1. Continue therapy q 3 weeks alternating ADR plus DTIC and CTX plus VCR.

For patients between 60 and 75 years of age: ADR - 35 mg/sqm, iv, on day 1, plus DTIC - 170 mg/sqm/day, iv, for days 1 through 5. CTX -800 mg/sqm, iv, on day 1, plus VCR - 1 mg/sqm, iv, on day 1. Continue therapy q 3 weeks alternating ADR plus DTIC and CTX plus VCR.

After the total dose of ADR has reached 550 mg/sqm, for both Arms, continue therapy with DTIC, VCR and CTX. Discontinue therapy in patients showing disease progression after 6 weeks of therapy. Continue therapy in responders or in patients with static disease for at least 2 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; DTIC - 100 and 200 mg vials; VCR - 1 mg vials; CTX - 100, 200, 500 and 1000 mg vials.

DATE SUMMARIZED: 01/77

10.0028 SURGERY WITH VS WITHOUT ADJUVANT CHEMOTHERAPY WITH ADR/DTIC/CTX/VCR FOR SOFT TISSUE SARCOMA

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PROTOCOL NUMBER(S) EORTC-62771

OBJECTIVES:

I. Study chemotherapy with adriamycin (ADR), DTIC, cyclophosphamide (CTX), and vincristine (VCR), as an adjunct to surgery in the management of soft tissue sarcoma of the extremities and of the head and neck region.

II. Compare the duration of the disease-free interval and survival in the group of patients being treated for 8 months and the patients given no chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients 20 to 70 years old with histologically proven soft tissue sarcomas with no metastatic disease. The bulk of the tumor must have been removed within 13 weeks of study entry. Patients must have adequate hematological and hepatic function, have had no prior radiotherapy nor chemotherapy nor macroscopic disease after tumor excision and no history of other malignant disease except skin cancer.

PROTOCOL OUTLINE: Randomized study. Randomize patients within 13 weeks of primary surgery or of resection of recurrent tumor.

Arm I: 4-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; DTIC, NSC-45388; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574.

Arm II: No Chemotherapy.

STRATIFICATION BY: Site of primary tumor: trunk and head and neck vs. limbs; prior radiotherapy; interval between surgery and start of chemotherapy: 8 weeks or less vs. 8 to 13 weeks; surgery for recurrent disease occurring more than 13 weeks after primary operation; intra-thoracal or intra-abdominal tumors; uterine sarcomas.

SPECIAL STUDY PARAMETERS: Lung tomography; skeletal scan.

END POINTS: Response/remission rate; recurrence rate, disease-free interval, duration of response; survival time.

CURRENT STATUS: 210 patients will be entered in less than 3 years.

DOSAGE SCHEDULE:

Arm I: ADR - 50 mg/sqm iv on day 1; DTIC - 400 mg/sqm iv push on days 1 through 3; CTX - 500 mg/sqm iv on day 1; VCR - 1.5 mg/sqm (maximum - 2 mg) iv on day 1. Repeat q 28 days for a total of 8 courses.

Follow up all patients 4 weeks. Remove patients with local recurrence or metastases from study. Randomize patients from Arm I to a phase II study. Cross over patients failing in Arm II to Arm I. Follow up all patients until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; DTIC - 100 and 200 mg vials; VCR - 1 mg vials; CTX - not given.

DATE SUMMARIZED: 05/79

10.0029 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED REFRACTORY SOFT TISSUE SARCOMA

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PROTOCOL NUMBER(S) EORTC-62793

OBJECTIVES:

I. Assess the objective antitumor activity of PALA in patients with advanced soft tissue sarcoma previously treated with chemotherapy.

II. Characterize the toxic effects of PALA.

PROTOCOL ENTRY CRITERIA: Patients with advanced soft tissue sarcoma who have failed to respond to conventional treatment. Patient must have a measurable lesion showing progression within 4 weeks prior to therapy. Patients must be between the ages of 15 and 75 years, have a Karnofsky index of at least 50 percent and have adequate hematologic, renal, and hepatic function. Patients must not have embryonal rhabdomyosarcoma, and there must be no CNS metastases, intercurrent infection, overt psychosis, or senility. Patients must receive no cytostatic agents within the 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic, renal, and hepatic function tests; urinalysis; chest x-rays; bone scan.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Initially 20 patients will be entered; for each response, 5 more will be entered, to a total of 40 patients.

DOSAGE SCHEDULE:

PALA - 2.5 g/sqm iv in a 60-minute infusion on days 1 and 2 q 2 weeks (i.e., on days 1, 2, 15, 16, etc.). Patients showing no response go off study after 6 courses; those showing tumor regression continue until progression and those showing tumor progression are given at least 3 courses, unless life-threatening toxicity develops. Patients stop treatment whenever severe toxicity develops despite dose reduction by 50%.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PALA - 10 ml ampules.

DATE SUMMARIZED: 10/80

10.0030 PHASE II CHEMOTHERAPY WITH ADRIAMYCIN VS CARMINOMYCIN FOR ADVANCED SOFT TISSUE SARCOMA

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PROTOCOL NUMBER(S) EORTC-62802

OBJECTIVES:

I. Assess the objective antitumor activity of carminomycin compared to adriamycin in patients with advanced soft tissue sarcoma previously untreated with cytotoxic agents.

II. Characterize further the toxic effects of carminomycin.

III. Look for cross resistance between anthracycline analogues by crossing patients resistant to carminomycin to adriamycin.

PROTOCOL ENTRY CRITERIA: Patients with confirmed residual or metastatic soft tissue sarcoma (Kaposi's sarcoma, chondro- and osteosarcoma are excluded), with a measurable lesion with progression. Patients must be between 15 and 80 years of age, have a Karnofsky performance status of at least 50 and have adequate hepatic, bone marrow, and cardiac function. Patients must have no overt psychoses, senility, acute intercurrent complications, CNS metastases, or previous/concomitant other malignant disease (except treated carcinoma in situ of cervix and carcinoma of the skin). Patients must have received no previous treatment with cytotoxic agents or radiotherapy to the indicator (for this study) lesion.

PROTOCOL OUTLINE: Randomized study. Patients who fail on Arm II cross over to Arm I.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: Single-agent Chemotherapy. Carminomycin, CMM, NSC-180024.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements, hematologic function tests, renal and hepatic function tests, chest x-ray, bone scan, ECG.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 58 patients (29 in each arm) will be entered. As of June 1980, 35 patients have been entered.

DOSAGE SCHEDULE:

Arm I: ADR - 75 mg/sqm rapid iv injection q 3 weeks, to a maximum cumulative dose of 550 mg/sqm.

Arm II: CMM - 20 mg/sqm rapid iv injection q 3 weeks, to a maximum cumulative dose of 150 mg/sqm.

After 2 courses patients in remission or with stable disease continue treatment until relapse. Patients on Arm I with progression discontinue treatment; patients on Arm II with progression cross over to Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 100 mg vials; CMM - 10.45 mg vials.

DATE SUMMARIZED: 10/80

10C. SARCOMA—GENERAL

10.0031 MASTER PROTOCOL AND PHASE II CHEMOTHERAPY WITH BLEO VS CLZ AND MGBG VS BRUCEANTIN FOR ADVANCED SOFT-TISSUE AND BONE SARCOMAS AND MESOTHELIOMAS

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PROTOCOL NUMBER(S) EST-1379

OBJECTIVES:

I. Determine activity of new agents and older compounds (bleomycin (BLEO) vs. chlorozotocin (CLZ) in this protocol) that have been inadequately evaluated in soft tissue sarcomas, bone sarcomas, mesotheliomas and other non-hematologic mesenchymal tumors. Sections 15 and 16 of the Master Protocol evaluating methyl-GAG (MGBG) and bruceantin (BRU) were activated in July 1980.

II. Compare response rate, response duration, and survival for each drug and the toxicity resulting from various drug regimens.

III. Determine whether there is a difference in response rate related to histopathologic type.

PROTOCOL ENTRY CRITERIA: Patients between 14 and 75 years of age with histologically confirmed and directly measurable residual, recurrent, or metastatic soft-tissue or bone sarcoma, mesothelioma, or other non-hematologic mesenchymal tumors. Previously irradiated tumors must show 25% increase in size. Patients must have an ECOG performance status of at least 3, and adequate hematologic, liver, and kidney functions. Patients may have any of the following histopathological tumor types: fibrosarcoma; spindle cell sarcoma; synovial cell sarcoma including malignant synovioma; malignant schwannoma including neurofibrosarcoma; malignant fibrous histiocytoma including malignant histiocytoma and fibroxanthosarcoma; leiomyosarcoma including malignant leiomyoblastoma; rhabdomyosarcoma including embryonal, alveolar, mixed, pleomorphic, and sarcoma botryoides; Kaposi's sarcoma; angiosarcoma; hemangiopericytoma; liposarcoma; osteosarcoma including parosteal sarcoma; chondrosarcoma; mesothelioma; sarcomas, type not designated; and all other sarcomas including epithelioid sarcoma, alveolar soft part sarcoma, malignant granular cell tumor, clear cell sarcoma of tendon and aponeurosis, small cell sarcoma, malignant giant tumor of soft parts. Patients must not have had prior chemotherapy with study drugs or a nitrosourea, no surgery or radiotherapy within the past 3 weeks (except to long bone only), and none to the lung or to the whole pelvis greater than 4000 rad. Patients who have progressed on EST-3377 are eligible, those with chronic pulmonary disease may enter Arm II only.

PROTOCOL OUTLINE: Randomized study. Arms III and IV added in July 1980.

Arm I: Single-agent Chemotherapy. Bleomycin, BLEO, NSC-125066.

Arm II: Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

Arm III: Single-agent Chemotherapy. Methyl-GAG, MGBG, NSC-32946.

Arm IV: Single-agent Chemotherapy. Bruceantin, BRU, NSC-165563.

STRATIFICATION BY: Participating institutions; ECOG performance status: 0 or 1 vs. 2 or 3; histopathologic type; prior therapy: Adriamycin vs. Adriamycin and/or other drugs.

SPECIAL STUDY PARAMETERS: Tumor measurements, performance status, chemistry profile.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 60 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BLEO - 20 U/sqm (maximum cumulative dose 240 U/sqm) iv on day 1 q 7 days for a minimum of 3 weeks.

Arm II: CLZ - 150 mg/sqm iv q 6 weeks for a minimum of 1 course. Give 120 mg/sqm to poor risk patients (between 65 and 75 years of age or with history of over 2500 rads to active marrow areas) until dosage is tolerated with acceptable toxicity.

Arm III: MGBG - 500 mg/sqm iv infusion over at least 45 minutes, weekly. In absence of toxicity, doses will be escalated in 50 mg/sqm weekly increments to a maximum of 700 mg/sqm. All patients receive minimum of 4 weekly doses unless serious toxicity intervenes; therapy continues until disease progression or unmanageable toxicity.

Arm IV: BRU - 5.5 mg/sqm on days 1, 8, 15, and 22 administered as a 4-hour infusion. Cycles repeated q 6 weeks.

All patients remain on study for minimum periods; thereafter patients remain on study until disease progression or development of unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 unit ampules; CLZ - 5 mg vials; MGBG - 1 g vials; BRU - 3 mg vials.

DATE SUMMARIZED: 10/79

10.0032 PHASE III CHEMOTHERAPY WITH ADR AND/OR PHASE II CHEMOTHERAPY WITH DBD, MTS OR ICRF-159 FOR SOFT TISSUE AND BONE SARCOMA AND MESOTHELIOMA

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PROTOCOL NUMBER(S) EST-3377

OBJECTIVES:

I. Compare the effectiveness of various adriamycin (ADR) induction regimens for soft tissue sarcomas, bony sarcomas and mesotheliomas.

II. Compare response rate, response duration, toxicity and survival of each induction regimen.

III. Define any differences in response rate which result from histopathologic type.

IV. Determine activity of dibromodulcitol (DBD), maytansine (MTS), and ICRF-159 (ICRF) in soft tissue sarcomas, bone sarcomas and mesotheliomasthat have progressed on other therapy including ADR.

PROTOCOL ENTRY CRITERIA: Patients 14 to 75 years old with measurable disease of histologically confirmed, residual, recurrent, or metastatic sarcoma, mesothelioma, or other nonhematologic mesenchymal tumor. (Patients with uterine leiomyosarcomas are eligible for entry. Addendum 3, December 1979.) Patients must have an ECOG performance status less than 4, adequate blood cell counts, creatinine less than 1.8 or BUN less than 25 mg%, bilirubin less than 2 mg%. Patients must not have had major surgical procedures or radiotherapy within the previous three weeks, or prior therapy to the pelvis greater than 4000 rads. If a lesion has been previously irradiated, it must show a 25% increase in size.

PROTOCOL OUTLINE: Randomized study.

Phase III study: Enter all patients with no prior Chemotherapy to Arm I, II, or III.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: Single-agent Chemotherapy. ADR, different schedule from Arm I.

Arm III: 2-Drug Combination Chemotherapy. ADR as in Arm I: DTIC, NSC-45388.

Phase II study: Enter all patients with prior Chemotherapy, including those who progress in the Phase III study, to Arm IV, V or VI.

Arm IV: Single-agent Chemotherapy. Dibromodulcitol, DBD, NSC-104800.

Arm V: Single-agent Chemotherapy. Maytansine, MTS, NSC-153858.

Arm VI: Single-agent Chemotherapy. ICRF-159, NSC-129943.

STRATIFICATION BY: Participating institutions; Phase III study: performance status, histopathology, site of measurable disease; Phase II study: performance status, histopathology, prior therapy.

SPECIAL STUDY PARAMETERS: Full lung tomography, left ventricular function.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: About 285 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Phase III study:

Arm I: ADR - 70 mg/sqm iv on day 1 q 21 days.

Arm II: ADR - 20 mg/sqm iv on days 1, 2 and 3, plus 15 mg/sqm iv on day 8. Repeat course q 7 days.

Arm III: ADR - 60 mg/sqm iv on day 1; DTIC - 250 mg/sqm iv on days 1 through 5. Repeat course q 21 days.

Suggested maximum total cumulative dose of ADR is 550 mg/sqm on all Arms. Upon exceeding this maximum dose, give DTIC - 250 mg/sqm iv on days 1 through 5 q 21 days or continue ADR at discretion of investigator.

Phase II study:

Arm IV: DBD - 180 mg/sqm po on days 1 through 10 q 28 days.

Arm V: MTS - 1.5 mg/sqm iv on day 1 q 21 days.

Arm VI: ICRF-159 - 900 mg/sqm po given in 3 divided doses on days 1, 2 and 3 q 28 days.

All patients remain on study 21 days. If disease progresses after 21 days in Phase III study, consider randomizing to Phase II study. Remove from protocol patients with disease progression after 21 days in Phase II study. Responders or patients with stable disease remain on study until progression occurs. Minimum adequate trials are 21 days for the Phase III study, 28 days for the Phase II study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; DTIC - 100 and 200 mg vials; MTX - 0.25 mg vials; ICRF-159 - 50, 250 and 500 mg tablets; DBD - 100 mg tablets.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00971178

10.0033 PILOT STUDY OF COMBINATION CHEMOTHERAPY WITH ADRIAMYCIN/CYCLOPHOSPHAMIDE/DTIC FOR METASTATIC SARCOMA

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PROTOCOL NUMBER(S) SEG-SAR-P27

OBJECTIVES:

I. Determine the complete and partial response rates of patients with advanced metastatic sarcoma to a combination of cyclophosphamide, DTIC and weekly, low-dose adriamycin (ADR).

II. Observe the effects of weekly ADR on electrocardiogram and echocardiogram done serially and whether patients carried beyond 600 mg/sqm develop congestive heart failure.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with advanced progressive metastatic sarcomas who have histological proof of a primary lesion and/or metastasis and at least 1 measurable lesion. Patients must have performance status above 40 and bilirubin no higher than 1.2. Patients must not have had prior treatment with study drugs. The following histological tumor types are eligible: liposarcoma, fibrosarcoma, leiomyosarcoma, rhabdomysarcoma, (pleomorphic or embryonal), sarcoma botryoides, synovial, osteogenic, Ewing's or giant cell sarcoma of bone, angiosarcoma, lymphangiosarcoma, chondrosarcoma, malignant schwannoma and other malignant neural tumors, alveolar soft part sarcoma, mesothelioma, uterine sarcomas other than leiomyosarcoma (mesodermal mixed tumors of uterus, carcinosarcoma of uterus) or other.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; DTIC, NSC-45388.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Skin tests for recall antigens, cardiac studies.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 25 evaluable patients will be entered.

DOSAGE SCHEDULE: ADR - 10 mg/sqm iv on days 1, 2, 3, 8, 9, 10, then 1 day q week starting on day 15; CTX - 600 mg/sqm iv on day 1 q 3 weeks; DTIC - 400 mg/sqm iv on days 1 and 2 q 3 weeks. Evaluate by day 63; remove patients who do not respond or have stable disease. Examine patients on therapy and those removed from treatment q 3 months for cardiac toxicity. Remove from study patients with disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; CTX - 100 mg vials; DTIC - 100 and 200 mg vials.

DATE SUMMARIZED: 10/78

10.0034 CHEMOTHERAPY WITH ADR/CTX/MTX VS ADR/CTX/MTX/AMPHOTERICIN-B & MAINTENANCE WITH ACT-D VS ACT-D/AMPHOTERICIN-B FOR METASTATIC SARCOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-78SAR0103; SEG-78SAR327

OBJECTIVES:

I. Compare the response rates of patients with metastatic sarcoma to a combination of adriamycin (ADR)/cyclophosphamide (CTX)/methotrexate (MTX) with or without amphotericin-B (AMB) as Induction therapy.

II. Compare the maximum quality of response and duration of response in patients treated with actinomycin-D (ACT-D) with or without AMB as Maintenance therapy.

III. Determine the response rate in patients with progressive disease after ADR/CTX/MTX when treated with AMB plus ADR/CTX/MTX.

PROTOCOL ENTRY CRITERIA: Patients with recently progressing, histologically proven, measurable advanced metastatic sarcoma which is not amenable to surgery or radiotherapy. Patients must be over 15 years of age with adequate renal and hepatic function. Patients must not have had prior therapy with ADR, CTX, MTX or ACT-D.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I: 3-Drug Combination Chemotherapy. ACM: Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740.

Arm II: 4-Drug Combination Chemotherapy. ACM plus Amphotericin-B, AMB, NSC-527017.

Cross over nonresponders. Rerandomize.

Maintenance:

Arm III: Single-agent Chemotherapy. Actinomycin-D, ACT-D, NSC-3053.

Arm IV: 2-Drug Combination Chemotherapy. ACT-D; AMB.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hepatic, renal, and bone marrow function.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, length of survival, duration of response, objective tumor response.

CURRENT STATUS: 180 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Induction:

Arm I: ADR - 60 mg/sqm (maximum dose 120 mg) iv on day 1; CTX -660 mg/sqm (maximum dose 1200 mg) iv on day 1; MTX - 25 mg/sqm (maximum dose 50 mg) iv on day 1. Repeat once on day 22. Three weeks later evaluate response and toxicity. Repeat course twice more for responding or stable patients q 21 days before re-evaluation and randomization to Maintenance. Cross over patients with progressive disease to Arm II.

Arm II: AMB - 7.5 mg/sqm iv on day 1, 15 mg/sqm iv on day 2, 30 mg/sqm iv on day 3; ADR - 40 mg/sqm iv on day 4; CTX - 400 mg/sqm iv on day 4; MTX - 20 mg/sqm iv on day 4. Repeat once on day 25. Three weeks later evaluate response and toxicity. Give responding or stable patients AMB-7.5 mg/sqm iv on day 1, 30 mg/sqm iv on day 2; ADR, CTX, MTX as above on day 2. Repeat q 21 days for two courses before re-evaluation and randomization to Maintenance. Remove from study patients showing progressive disease.

Maintenance:

Arm III: ACT-D - 2 mg/sqm iv q 28 days. Reinduce patients showing progressive disease in the same Arm as their initial therapy.

Arm IV: AMB - 15 mg/sqm iv on day 1; ACT-D - 2 mg/sqm iv after AMB on day 1. Repeat q 28 days for 7 courses, then omit AMB and continue ACT-D q 28 days. Reinduce patients with progressive disease in the same Arm as their initial therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200 and 500 mg vials; MTX - 5 and 50 mg vials; ACT-D - 0.5 mg vials; AMB - 50 mg vials.

DATE SUMMARIZED: 10/78

PATIENT ACCRUAL: 00200978

10.0035 PHASE II CHEMOTHERAPY WITH CHLOROZOTOCIN FOR ADVANCED SARCOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7982

OBJECTIVES:

I. Determine whether chlorozotocin in a dose of 120 mg/sqm has significant activity in sarcoma by determination of response rate and duration.

II. Describe toxicities of chlorozotocin not yet defined.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven advanced bony or soft tissue sarcoma, who are not candidates for known regimens or protocols of higher efficacy or priority, with measurable disease, an expected survival of at least 6 weeks, and adequate bone marrow function. They must be beyond the nadir of myelosuppression resulting from prior chemotherapy or radiotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: BUN and creatinine, SGOT, SGPT, LDH, chest x-ray or scans, Karnofsky performance status.

END POINTS: Objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 25 patients will be entered; it is expected that one year will be required for accrual of this number. Further accrual of patients will be based on examination of data.

DOSAGE SCHEDULE:

CLZ - 120 mg/sqm iv bolus initially, repeated every 6 weeks. Subsequent courses will be given to those patients achieving a tumor response or stable disease, provided hematologic recovery has occurred: WBC equal to or greater than 4000 and platelets 100,000. Treatment will be withheld until these counts are reached. Patients who develop diabetes mellitus or other non-hematologic toxicities considered secondary to the CLZ shall be continued in treatment only if there is unequivocal response to CLZ.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLZ - 50 mg vials.

DATE SUMMARIZED: 05/80

10.0036 PHASE II CHEMOTHERAPY WITH DIHYDROXYANTHRACENEDIONE FOR SOFT TISSUE AND BONE SARCOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-8004

OBJECTIVES:

I. Determine the efficacy, by response rate, of dihydroxyanthracenedione (DHAD) in patients with soft tissue and bone sarcoma, who have failed on higher priority treatment protocols.

II. Determine the nature and degree of toxicity of this drug used in a single-dose schedule with 3-week intervals.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven incurable soft tissue or bone sarcoma with clearly measurable disease who are not eligible for higher priority SWOG studies. Patients must have a life expectancy of at least 6 weeks and a performance status of 3 or better (Karnofsky greater than 30). The WBC count must be at least 3500/cumm; the platelet count must be equal to or greater than 125,000/cumm. Serum creatinine and serum bilirubin must be equal to or less than 2 mg percent. No other chemotherapeutic agent or radiotherapy may be given concomitantly.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests, tumor measurement.

END POINTS: Objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 25 patients will be entered; if no response is seen in first 14 evaluable patients, accrual will be terminated.

DOSAGE SCHEDULE:

DHAD - 12 mg/sqm through a free running iv over 30 minutes. Repeat q 3 weeks provided patient has recovered from previous drug-induced toxicity. Patients with progressive disease after 1 or more courses and patients who develop unacceptable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 5 mg ampules.

DATE SUMMARIZED: 10/80

10.0037 PHASE II INDUCTION WITH BLEO/CTX/ADR/CACP AND CONSOLIDATION WITH ALTERNATING VCR/CTX/ACT-D AND VCR/ADR/DTIC FOR ADVANCED SARCOMAS

Edmonson, J. H., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-797701

OBJECTIVES:

I. Determine effect of combination chemotherapy induction with bleomycin (BLEO)/cyclophosphamide (CTX)/adriamycin (ADR)/-cis-platinum (CACP) and consolidation with alternating vincristine (VCR)/CTX/actinomycin D (ACT-D) and VCR/ADR/DTIC for advanced sarcomas.

PROTOCOL ENTRY CRITERIA: Patients under 75 years of age with histologically confirmed, measurable or evaluable, advanced sarcoma for which no curative treatment is known. Patients must have: expected survival of at least 2 months, ECOG performance status of at least 3, adequate hematologic and kidney function, and normal liver function.

PROTOCOL OUTLINE: Nonrandomized study.

Induction:

4-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

Consolidation: Enter all patients who have not experienced progression by 1 month after first day of Induction.

3-Drug Alternating Combination Chemotherapy. Vincristine, VCR, NSC-67574; CTX; Actinomycin D, ACT-D, NSC-3053 alternating with VCR; ADR; DTIC, NSC-45388.

STRATIFICATION BY: Chemotherapy: prior vs. no prior; histological grade: 1 or 2 vs. 3 or 4; tissue of origin: visceral vs. soft tissue and bone.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 20 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Induction:

BLEO - 20 U/sqm (maximum cumulative dose 240 U/sqm or 400 U regardless of size) iv over 24 hrs in 3000 ml D5W on days 1, 2, and 3; CTX - 400 mg/sqm iv push on day 1; ADR - 40 mg/sqm iv over 5 to 10 min on day 1; CACP - 60 mg/sqm iv over 2 hrs in 1000 ml 1/2N saline and 25 gm mannitol on day 1. Continue Induction for a total of 4 monthly cycles, unless progression occurs earlier.

Consolidation:

VCR - 1.2 mg/sqm (maximum dose 2 mg) iv push on days 1 and 5; CTX - 250 mg/sqm iv push on days 1, 3, and 5; ACT-D - 0.325 mg/sqm iv push on days 1 through 5; alternately with VCR - 1.2 mg/sqm (maximum dose 2 mg) iv push on days 1 and 5; ADR - 50 mg/sqm iv over 5 to 10 min on day 3; DTIC - 250 mg/sqm iv over 20 to 30 min on days 1 through 5.

Remove from study patients in progression during Consolidation if they resist reinduction with CTX/ADR/CACP or patients who have reached maximum allowable cumulative dose of ADR (520 mg/sqm). Continue Consolidation regimen without ADR for patients who have not progressed after 18 months of chemotherapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 U ampules; VCR - 1 and 5 mg ampules; CTX - 100, 200, and 500 mg vials; ADR - 10 mg vials; CACP - 10 mg vials; ACT-D - 0.5 mg vials; DTIC - 100 and 200 mg vials.

DATE SUMMARIZED: 02/80

10.0038 PHASE II CHEMOTHERAPY WITH AMSA FOR REFRACTORY METASTATIC SARCOMA

Yap, B., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-271; MDA-DT-7815

OBJECTIVES:

I. Determine the efficacy of AMSA in the treatment of refractory metastatic sarcomas.

II. Determine the qualitative and quantitative toxicity of this drug.

PROTOCOL ENTRY CRITERIA: Patients with measurable, metastatic, biopsy-confirmed soft tissue or bone sarcoma who have failed after surgery or higher priority chemotherapy. Patients must have a minimum life expectancy of 10 weeks and have adequate bone marrow, liver and renal function. Patients must be off radiation and chemotherapy for at least 3 weeks and have recovered from toxicity.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: SMA-100, PPT.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 27 evaluable patients as of June 1979.

DOSAGE SCHEDULE:

AMSA - 40 mg/sqm iv on days 1 through 3. Dosage changed to 120 mg/sqm iv single dose q 3 weeks (100 mg/sqm for patients with inadequate marrow reserve) Abstract, April 1978. Further increased to 150 mg/sqm q 3 weeks (120 mg/sqm for inadequate marrow reserve patients), Protocol update, June 1979. Repeat course q 3 weeks for at least 2 courses. Remove from study patients with progressive disease, unacceptable status or toxicity.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 09/79

PATIENT ACCRUAL: 00270679

10.0039 PHASE II CONTINUOUS 5-DAY INFUSION CHEMOTHERAPY WITH DAVA VS VBL FOR REFRACTORY METASTATIC SARCOMA

Yap, B. S., (713-792-2121) University of Texas, Cancer Center, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-331; MDA-DT-7901

OBJECTIVES:

I. Compare the effects of continuous 5-day infusion chemotherapy with vindesine (DAVA) vs. vinblastine (VBL).

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed soft tissue or bone sarcoma with measurable metastases who have already received appropriate surgical therapy and who have failed on regimens of higher priority. Patients must have a life expectancy of at least 10 weeks and adequate bone marrow, liver, and kidney function. Patients must not have had chemotherapy or radiotherapy in the preceding 3 weeks nor have remaining evidence of toxicity.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

Arm II: Single Agent Chemotherapy. Vinblastine, VBL, NSC-49842.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 50 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Arm I: DAVA - 1.2 mg/sqm iv continuous infusion on days 1 through 5.

Arm II: VBL - 1.5 mg/sqm iv continuous infusion on days 1 through 5.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

10.0040 PHASE II CHEMOTHERAPY WITH PALA FOR REFRACTORY METASTATIC SARCOMA

Yap, B. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States America

PROTOCOL NUMBER(S) MDAR-396; MDA-DT-8015

OBJECTIVES:

I. Determine the efficacy of a single or multiple dose schedule of PALA in patients with refractory metastatic soft tissue and bone sarcoma who have failed on higher priority treatment protocols including adriamycin-containing regimens.

II. Determine the qualitative and quantitative toxicity of PALA when administered in this fashion.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven advanced soft tissue and bone sarcoma, with clearly measurable disease, who are not eligible for higher priority Southw Oncology Group studies. Patients must have a life expectancy of least 6 weeks; a Karnofsky performance status of at least 50-60; an adequate hematologic, renal and hepatic function. Patients must not have received chemotherapy or radiotherapy for four weeks prior to entry.

PROTOCOL OUTLINE: Randomized study. Arm II discontinued November 1980.

Arm I: Single-agent Chemotherapy. Single-dose schedule. PALA, NSC-224131.

Arm II: Single-agent Chemotherapy. Multiple-dose schedule PALA.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, disease-free interval, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: PALA - 6 g/sqm iv on day 1 q 2 weeks.

Arm II: PALA - 1 g/sqm iv daily on days 1 through 5 q 2 weeks. Arm discontinued November 1980.

All patients receive at least 2 courses of Chemotherapy. Treatment will continue for 2 years or for 1 year after achieving CR, whichever is shorter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

10.0041 PHASE II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR ADVANCED SOFT TISSUE AND BONE SARCOMA

Yap, B. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-417; MDA-DT-8036

OBJECTIVES:

I. Determine the efficacy of anthracenedione administered by a single intravenous schedule to patients with advanced soft tissue and bone sarcoma.

II. Determine the qualitative and quantitative toxicity of anthracenedione administered in this fashion.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-confirmed diagnosis of soft tissue or bone sarcoma with measurable lesions and measurable metastases, who have already received appropriate surgical therapy and who have failed on regimens of higher priority. Patients must have a life expectancy of at least 10 weeks and be at least 16 years of age. Patients must have adequate bone marrow, liver and renal function, unless therapy is indicated as a life-saving measure; they must not receive chemotherapy or radiotherapy for at least 3 weeks prior to entry and must show no evidence of toxicity.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Anthracenedione, Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Granulocyte and platelet counts.

END POINTS: Response/remission rate, duration of response, disease-free interval, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 14 evaluable patients will be entered.

DOSAGE SCHEDULE:

DHAD - 12 mg/sqm iv over 30 minutes q 3 to 4 weeks. Chemotherapy is continued for a total period of 2 years, or one year after achieving complete remission, whichever is shorter. Therapy is withdrawn when unacceptable gastrointestinal side effects, hematopoietic suppression, or any other untoward effects develop.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/80

10.0042 PRIMARY RADIOTHERAPY AND RADIOSENSITIZATION WITH MISONIDAZOLE FOR UNRESECTABLE OSTEOGENIC SARCOMA AND CHONDROSARCOMA

Glatstein, E., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-78-C-101

OBJECTIVES:

I. Evaluate the therapeutic efficacy of atypically fractionated radiotherapy combined with misonidazole in achieving local control of osteogenic sarcoma and chondrosarcoma that are not amenable to surgery.

II. Assess survival in these patients and analyze sites of failure.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented osteogenic sarcoma and chondrosarcoma whose local tumor mass is beyond surgical therapy. Hepatic, renal, and bone marrow functions must be adequate, and there may be no distant metastases or second active tumor.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy with Radiosensitization. Megavoltage techniques plus Misonidazole, MNI, NSC-261037.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Total tumor dose of 5000 rads delivered in 500-rad fractions twice weekly for a total of 10 fractions. MNI - 2 g/sqm po 4 hours prior to each Radiotherapy treatment. Patients receive physical therapy before, during, and after treatment. Patients may also receive Chemotherapy according to other NCI protocols.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

10.0043 CHEMOTHERAPY WITH ADR, MTX WITH & WITHOUT ADJUVANT IMMUNOTHERAPY WITH BCG & ALLOGENEIC TUMOR CELL VACCINE IN SKELETAL & SOFT TISSUE SARCOMA

Eilber, F. R., (213-825-7081) University of California, Los Angeles, Division of Oncology, Dept. of Surgery, 924 Westwood, Suite 400, Los Angeles, California, 90024, United States of America
PROTOCOL NUMBER(S) UCLA-SAR-1

OBJECTIVES:

I. Compare the efficacy of adjuvant immunotherapy with BCG and allogeneic tumor cell vaccine plus chemotherapy with adriamycin (ADR) and high-dose methotrexate (MTX) to chemotherapy alone in patients with skeletal and soft tissue sarcoma.

II. Compare the improvement in disease-free and overall survival between these two regimens.

PROTOCOL ENTRY CRITERIA: Patients with Stage I, Grade III skeletal sarcoma.

PROTOCOL OUTLINE: Randomized study. Patients randomized after surgery.

Arm I: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; high-dose Methotrexate, HD-MTX, NSC-740.

Arm II: 2-Drug Combination Chemotherapy plus Immunotherapy. ADR; MTX; plus BCG-Tice, BCG, NSC-B116327, and allogeneic tumor cell vaccine.

STRATIFICATION BY: Age, sex, site of primary tumor, histologic grade.

SPECIAL STUDY PARAMETERS: Skin test reactivity, toxicity of chemotherapy (nadir of WBC, total dose administered).

END POINTS: Minimum of 20 percent difference in disease-free or overall survival.

CURRENT STATUS: 110 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: ADR - 90 mg/sqm iv once/month, for 6 months; HD-MTX - 200 mg/kg iv once/month, for 12 months.

Arm II: ADR, HD-MTX, as in Arm I. BCG - one ampule per treatment, id by tine technique q 2 weeks for 2 years; irradiated tumor cell vaccine, 100 million cells, intradermal in 4 sites each treatment, q 2 weeks for 2years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 01100280

SECTION 11

PEDIATRIC SOLID TUMORS

11A. WILMS' TUMOR

COSTA-RICA-W278 TREATMENT OF NEPHROBLASTOMA (WILMS' TUMOR) BY COMBINED CHEMOTHERAPY WITH ACT-D/ADR/VCR, SURGERY AND RADIOTHERAPY 11.0001

11B. NEUROBLASTOMA

CCG-371 PHASE III CHEMOTHERAPY WITH SEQUENTIAL CTX/ADR WITH/WITHOUT VM-26 AND CPDD PLUS CYCLIC VCR/CTX/DTIC FOR CHILDHOOD METASTATIC NEUROBLASTOMA 11.0002

CCG-372 PHASE II COMBINATION CHEMOTHERAPY WITH CIS-PLATINUM/VM-26 FOR RECURRENT STAGE IV NEUROBLASTOMA OF CHILDHOOD 11.0003

CCG-373 PHASE III CYCLIC COMBINATION CHEMOTHERAPY WITH CTX/DTIC/VCR AND ADR/CTX PLUS RADIOTHERAPY FOR STAGE III NEUROBLASTOMA 11.0004

CLB-7541 PHASE III CHEMOTHERAPY WITH VCR/CTX/ADR, RADIOTHERAPY AND MER-BCG IMMUNOTHERAPY FOR NEUROBLASTOMA, STAGES III AND IV 11.0005

SWOG-7875 PHASE I-II COMBINATION CHEMOTHERAPY WITH ADR/CACP/VCR/CTX FOR METASTATIC NEUROBLASTOMA 11.0006

SWOG-8002 COMBINATION CHEMOTHERAPY WITH ADR/CTX/CACP/VCR FOR PEDIATRIC METASTATIC STAGE IV NEUROBLASTOMA 11.0007

SJCRH-NB-2 SURGERY, CHEMOTHERAPY AND RADIOTHERAPY WITH MAINTENANCE IMMUNOTHERAPY FOR NEUROBLASTOMA 11.0008

SJCRH-NB-79 SURGERY AND CHEMOTHERAPY WITH CTX, ADR, CACP, AND VM-26 FOR NEUROBLASTOMA 11.0009

11C. RHABDOMYOSARCOMA

NCI-76-C-385 PRE- VS POSTOPERATIVE CHEMOTHERAPY FOR STAGES I-II RHABDOMYOSARCOMA AND INTENSIVE ESCALATING PREOPERATIVE CHEMOTHERAPY FOR STAGE III DISEASE 11.0010

SJCRH-RMS-3 SURGERY, RADIOTHERAPY AND COMBINATION CHEMOTHERAPY WITH CTX/ADR/VCR/ACT-D FOR CHILDHOOD RHABDOMYOSARCOMA 11.0011

11D. EWING'S SARCOMA

SWOG-7895 VCR, CTX, ADR, ACT-D CHEMOTHERAPY AND/OR RADIOTHERAPY AND/OR SURGERY FOR PRIMARY LOCALIZED EWING'S SARCOMA OF PELVIC AND SACRAL BONES 11.0012

SWOG-8095 PHASE III COMBINATION CHEMOTHERAPY PLUS RADIOTHERAPY AND SURGERY FOR METASTATIC EWING'S SARCOMA 11.0013

NCI-77-C-150 PROPHYLACTIC PULMONARY IRRADIATION PLUS PRIMARY SITE IRRADIATION AND VAC/VADRC COMBINATION CHEMOTHERAPY FOR LOW-RISK EWING'S SARCOMA 11.0014

NCI-77-C-165 TBI PLUS CHEMOTHERAPY WITH VADRC (VCR/ADR/CTX) AND HIGH DOSE VCR/ADR/CTX/DTIC FOR METASTATIC AND HIGH RISK EWING'S SARCOMA 11.0015

NCI-77-C-167 HIGH-DOSE CHEMOTHERAPY WITH VAC (VCR/ACT-D/CTX) PLUS DTIC OR VADRC (VCR/ADR/CTX) PLUS DTIC FOR RECURRENT EWING'S SARCOMA 11.0016

SJCRH-EWI-79 INDUCTION WITH CTX/ADR, MAINTENANCE WITH VCR/ACT-D/BCNU/CTX/ADR AND DELAYED RADIOTHERAPY FOR EWING'S SARCOMA ... 11.0017

COSTA-RICA-PE278 PILOT STUDY TREATMENT OF EWING'S TUMOR WITH RADIOTHERAPY, SURGERY, AND CHEMOTHERAPY WITH ACT-D/CTX/VCR/ADR/MTX 11.0018

11E. PEDIATRIC SOLID TUMORS—GENERAL

CCG-074 PHASE II CHEMOTHERAPY WITH HIGH DOSE HEXAMETHYLMELAMINE FOR RESISTANT CHILDHOOD LYMPHOMAS AND OTHER SOLID TUMORS 11.0019

SWOG-7607B PHASE II CHEMOTHERAPY WITH ADCONFU (ADR/CTX/VCR/5-FU) PLUS LITHIUM CARBONATE FOR NONRESECTABLE SOLID TUMORS IN CHILDREN 11.0020

SWOG-7617 CHEMOTHERAPY WITH VBL/BLEO FOR METASTATIC SOLID TUMORS IN CHILDREN 11.0021

SWOG-7843 PHASE II CHEMOTHERAPY WITH RUBIDAZONE FOR SOLID TUMORS IN CHILDREN 11.0022

SWOG-8018 PHASE II CHEMOTHERAPY WITH M-AMSA FOR CHILDREN WITH SOLID TUMORS 11.0023

NCI-76-C-203 PARENTERAL HYPERALIMENTATION AS ADJUVANT TO AGGRESSIVE CHEMOTHERAPY IN RHABDOMYOSARCOMA AND NEUROBLASTOMA 11.0024

NCI-78-C-140 PHASE II TRIAL OF ISOPHOSPHAMIDE IN REFRACTORY PEDIATRIC MALIGNANCIES 11.0025

NCI-79-C-23 PHASE II IMMUNOTHERAPY WITH STABILIZED POLY IC IN THE TREATMENT OF REFRACTORY PEDIATRIC SOLID TUMORS 11.0026

COSTA-RICA-P01179 SURGERY COMBINED WITH CTX/MTX/CF/ADR FOR OSTEOSARCOMA IN CHILDREN 11.0027

SECTION 11

PEDIATRIC SOLID TUMORS

11A. WILMS' TUMOR

11.0001 TREATMENT OF NEPHROBLASTOMA (WILMS' TUMOR) BY COMBINED CHEMOTHERAPY WITH ACT-D/ADR/VCR, SURGERY AND RADIOTHERAPY

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PROTOCOL NUMBER(S) COSTA-RICA-W278

OBJECTIVES:

I. Relate tumor spread and the patient's age with a treatment combining surgery, irradiation and chemotherapy.

II. Demonstrate that for children of any age in Stages IA and B (tumor localized in the kidney), radiotherapy can be omitted without detriment to survival, therapy avoiding the sequelae that it so often leaves in these patients.

III. Administer a chemotherapy in which the choice of drugs, the dosages and the duration of administration are tailored to the stage of the tumor, and which provides longer survival with fewer complications and sequelae.

IV. Determine whether adriamycin increases the frequency and duration of remission in Stages III and IV.

V. Begin a study of tumor histology to evaluate the influence of anaplasia and predominance of sarcomatous tissue on the prognosis.

PROTOCOL ENTRY CRITERIA: Patients with demonstrable Wilms' embryoma (nephroblastoma), Stages I through V, resectable or nonresectable, metastatic or not.

PROTOCOL OUTLINE: Nonrandomized study. Patients assigned to various treatments on basis of clinical stage of tumor.

Stage I-A: Single-agent Chemotherapy. Actinomycin-D, ACT-D, NSC-3053.

Stage I-B: 2-Drug Combination Chemotherapy. ACT-D; Vincristine, VCR, NSC-67574.

Stage II-A: Radiotherapy plus 2-Drug Combination Chemotherapy. ACT-D, VCR. Radiotherapy - renal area.

Stage II-B: Radiotherapy plus 2-Drug Combination Chemotherapy. ACT-D, VCR. Radiotherapy - renal cavity.

Stage III: Radiotherapy plus 3-Drug Combination Chemotherapy. ACT-D; VCR; Adriamycin, ADR, NSC-123127. Radiotherapy individually dosed.

Stage IV: Radiotherapy plus 3-Drug Combination Chemotherapy. ACT-D; VCR; ADR. Presurgical radiotherapy of pulmonary and hepatic metastases.

STRATIFICATION BY: Participating institutions, extent of tumor, site and extent of tumor metastases.

SPECIAL STUDY PARAMETERS: Catecholamines in urine, renal and hepatic mapping, creatinine clearance in cases of bilateral tumors, complete coagulation tests in metastatic patients.

END POINTS: Toxicity/morbidity of treatment, objective tumor response, response/remission rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Stage I-A: No Radiotherapy. ACT-D - 15 mg/kg/day/5 days iv (transoperative period); 400 mg/sqm iv days 13, 20, 27, 34, 41 and 48.

Stage I-B: No Radiotherapy. ACT-D - 15 mg/kg/day/5 days iv, 400 mg/sqm iv days 13, 20, 27, 34, 41 and 48, plus VCR - 1.5 mg/sqm iv same days.

Stage II-A: Radiotherapy renal area, 2500 rad, expanding field from 2 to 4 cm, beginning on day 8 following surgery. ACT-D plus VCR same dosage as in Stage I-B, but extended beyond 6 weeks for total of 20 semi-weekly doses.

Stage II-B: Radiotherapy of renal cavity, 2500 rad, expanding field of 4 cm, beginning 8 days after surgery. Transoperative ACT-D - 600 mg/sqm iv plus VCR for 6 weeks, then 30 semi-weekly doses.

Stage III: Radiotherapy individually dosed, between 2000 and 3500 rad depending on age and condition of patient, and tumor size. Drugs same as in Stage II-B, plus ADR - 30 to 40 mg/sqm iv for total dose of 300 mg/sqm over 6-week period; suspend ACT-D and VCR when administering ADR.

Stage IV: Radiotherapy of pulmonary and hepatic metastases before surgery. If complete or partial remission (reduction of more than 50 percent in volume of metastases) has been accomplished, extirpation of tumor, with lymphadenectomy and partial hepatectomy if necessary, is performed. ACT-D - 600 mg/sqm iv for 30 semi-weekly doses; VCR - 1.5 mg/sqm iv for 72 weekly doses; ADR - q 4 weeks up to total dose of 300 mg/sqm. On days when ADR is injected, no ACT-D or VCR will be administered.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

11B. NEUROBLASTOMA

11.0002 PHASE III CHEMOTHERAPY WITH SEQUENTIAL CTX/ADR WITH/WITHOUT VM-26 AND CPDD PLUS CYCLIC VCR/CTX/DTIC FOR CHILDHOOD METASTATIC NEUROBLASTOMA

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PROTOCOL NUMBER(S) CCG-371

OBJECTIVES:

I. Determine effect of combination chemotherapy with cycles of vincristine (VCR)/cyclophosphamide (CTX)/DTIC vs. cycles of VCR/CTX/DTIC plus sequential CTX/adriamycin (ADR) vs. cycles of VCR/CTX/DTIC plus sequential CTX/ADR/VM-26 on newly-diagnosed, Stage IV, childhood neuroblastoma. (Cis-platinum, CPDD, added to the CTX/ADR/VM-26 combination–Addendum 2, March 1980.)

II. Determine whether factors other than age at diagnosis are important prognostic factors.

PROTOCOL ENTRY CRITERIA: Patients under 16 years of age with newly-diagnosed, Stage IV (not IV-S), histologically-confirmed (or clumps of tumor cells in bone marrow and elevated urine catecholamines) neuroblastoma.

PROTOCOL OUTLINE: Randomized study for Induction and Maintenance only.

Regimen A: 3-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; DTIC, NSC-45388.

Induction and Maintenance:

Arm I: 3-Drug Combination Chemotherapy. VCR; CTX; DTIC.

Arm II: 4-Drug Combination Chemotherapy. VCR; CTX; DTIC; Adriamycin, ADR, NSC-123127.

Arm III: 5-Drug Combination Chemotherapy. VCR; CTX; DTIC; ADR; VM-26, NSC-122819; cis-Platinum, CPDD, NSC-119875. (CPDD per Addendum 1, March 1980)

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Lesion measurement, bone marrow aspirate and biopsy, liver function, urinalysis, radiological and radioisotopic survey, lumbar puncture, urine catecholamines.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 160 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Regimen A: VCR - 1.5 mg/sqm iv on day 5; CTX - 750 mg/sqm iv on day 1; DTIC - 250 mg/sqm iv on days 1 through 5. All on weeks 1, 4, and 7.

Induction and Maintenance: At week 10 randomize all patients with complete or partial response to Arms I, II, and III. Evaluate patients at 22 weeks for entrance to Maintenance. Patients with complete response are eligible for Maintenance if there is no residual disease following surgery for resection of lesions. If there is residual disease following surgery, enter patients to Maintenance after Radiotherapy: megavolt radiation of 2400 to 3000 rads to primary lesion and 600 to 3000 rads to metastatic sites. For patients with partial response or stable disease at week 22, continue Induction therapy for 9 more weeks; then enter to Radiotherapy as above. Following this Radiotherapy, enter to Maintenance: patients with complete response or partial response without metastatic disease after surgery for resection of lesions; and enter patients with partial response with metastatic disease or with stable disease directly. Continue Chemotherapy for all patients during Radiotherapy. Remove from study patients with progressive disease at any time during the study, except give Radiotherapy to patients who develop progressive disease after initial response prior to week 22. Discontinue therapy for all patients who are tumor-free for 2 years.

Arm I: VCR; CTX; DTIC as in Regimen A q 3 weeks starting with week 10 and ending with week 103.

Arm II: VCR; CTX; DTIC as in Arm I; CTX - 150 mg/sqm po on days 1 through 7; ADR - 35 mg/sqm iv on day 8; both on weeks 10, 16, 31, 52, 58, 73, 79, 94, and 100.

Arm III: VCR; CTX; DTIC; CTX; ADR, all as in Arm II; CPDD (Addendum 1, March 1980) - 3 mg/kg iv on day 1; VM-26 - 150 mg/sqm iv on days 2, 9, and 16 on weeks 13, 19, 34, 40, 55, 61, 76, 82, 97, and 103.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CTX - 100 and 500 mg vials, 25 and 50 mg tablets; DTIC - 200 mg vials; ADR - 10 mg vials; VM-26 - 50 mg ampules; CPDD - 10 mg vials.

DATE SUMMARIZED: 04/80

11.0003 PHASE II COMBINATION CHEMOTHERAPY WITH CIS-PLATINUM/VM-26 FOR RECURRENT STAGE IV NEUROBLASTOMA OF CHILDHOOD

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PROTOCOL NUMBER(S) CCG-372

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with cis-platinum/VM-26 for childhood recurrent Stage IV neuroblastoma.

PROTOCOL ENTRY CRITERIA: Patients under 18 years of age with recurrent Stage IV neuroblastoma. Patients must have measurable disease and/or elevated urinary catecholamines and one index lesion which will not receive Radiotherapy, normal renal function and calcium and magnesium levels, granulocyte count greater than 1500, and platelet count greater than 75,000.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; VM-26, VM-26, NSC-122819.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Audiography, radionuclide scans, bone marrow aspirate, serum electrolytes, calcium and magnesium levels.

END POINTS: Objective tumor response, duration of remission, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

CACP - 3 mg/kg iv, on day 0 in an 8-hour infusion with Mannitol - 250 mg/kg on day 0 q 3 weeks; VM-26 - 150 mg/sqm iv on days 1 (day 2, Addendum 2, November 1979), 8, and 15. Cycles repeated q 3 weeks; 2 cycles considered adequate trial.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; VM-26 - 50 mg ampules.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00480279

11.0004 PHASE III CYCLIC COMBINATION CHEMOTHERAPY WITH CTX/DTIC/VCR AND ADR/CTX PLUS RADIOTHERAPY FOR STAGE III NEUROBLASTOMA

Hammond, S., (213-226-2008) Childrens Cancer Study Group, c/o U. of S. Calif. Canc. Ctr., 1721 Griffin Ave., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-373

OBJECTIVES:

I. Determine the degree of decrease in the size of the tumor after three courses of cyclophosphamide (CTX), DTIC, and vincristine (VCR), and whether additional reduction can be obtained with radiotherapy.

II. Determine at second-look surgery following chemotherapy and irradiation the number of complete remissions and the resectability of the tumor.

III. Determine whether selected 'front-end' factors other than age at diagnosis are important prognostic factors in Stage III neuroblastoma.

IV. Correlate with prognosis the presence or absence of lymph node metastasis and complete resection at time of diagnosis.

V. Determine whether or not the addition of cycles of adriamycin (ADR) and CTX to CTX, DTIC, and VCR will improve disease-free survival time.

PROTOCOL ENTRY CRITERIA: Patients 1-21 years of age with Stage III neuroblastoma. Patients must be newly diagnosed and they must not have received chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 3-Drug Combination Chemotherapy plus Radiotherapy plus Surgery. Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; DTIC, NSC-45388. Megavoltage radiation plus VCR.

Maintenance: 4-Drug Combination Chemotherapy. VCR; CTX; DTIC; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Complete blood count, liver and renal function tests, CT scan and/or ultrasound examination of the area of the primary tumor, urinary catecholamines.

END POINTS: Duration of response, objective tumor response, length of survival, disease-free interval, toxicity/morbidity of treatment.

CURRENT STATUS: 60 patients will be entered over a 3-year period.

DOSAGE SCHEDULE:

Induction: Enter all patients within one week of surgery. VCR - 1.5 mg/sqm iv (maximum 2.0 mg) on day 5 of weeks 1, 4, and 7; CTX - 750 mg/sqm iv on day 1 of weeks 1, 4, and 7; DTIC - 250 mg/sqm iv on days 1 through 5 of weeks 1, 4, and 7. Evaluate for tumor size on week 10. VCR - 1.5 mg/sqm iv on day 1 of weeks 10, 11, and 12. 2400-4000 rads given as 150-200 rads/day doses to primary site on weeks 10, 11, and 12 (total dosage age-dependent). Evaluate for tumor size on week 14. VCR, CTX, and DTIC given as before but on weeks 14 and 17. Evaluate for second-look surgery on week 19; patients with progressive disease go off study.

Maintenance: VCR - 1.5 mg/sqm iv on day 5 of weeks 24, 30, 33, 36, 42, 48, 51, 54, 60, 66, 69, 72, 78, 84, 87, and 90. CTX - 750 mg/sqm iv on day 1 of same weeks as VCR; DTIC - 250 mg/sqm iv on days 1 through 5 of same weeks as VCR; CTX - 150 mg/sqm po on days 1 through 7 of weeks 21, 27, 39, 45, 57, 63, 75, and 81; ADR - 35 mg/sqm iv once weekly in same weeks as CTX.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials and 25 and 50 mg tablets; VCR - 1.0 and 5.0 mg vials; DTIC - 200 mg vials; ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 10/80

11.0005 PHASE III CHEMOTHERAPY WITH VCR/CTX/ADR, RADIOTHERAPY AND MER-BCG IMMUNOTHERAPY FOR NEUROBLASTOMA, STAGES III AND IV

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PROTOCOL NUMBER(S) CLB-7541

OBJECTIVES:

I. Evaluate the role of triple-drug (vincristine, cyclophosphamide, adriamycin) combination chemotherapy in previously untreated stage III and IV neuroblastoma.

II. Evaluate the immunological responsiveness of patients with disseminated neuroblastoma, both prior to and during therapy.

III. Evaluate MER-BCG as a stimulant of immunological responsiveness both in terms of the patient's immunological reactivity (to skin tests) and in terms of possible contribution to prolongation of median survival.

PROTOCOL ENTRY CRITERIA: Children above age 1 with measurable lesions of neuroblastoma Stage III or IV and who have not received prior chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

Arm II: 3-Drug Combination Chemotherapy plus Immunotherapy. Arm I chemotherapy plus MER-BCG, NSC-143679.

Arm III: Radiotherapy. Supervoltage radiotherapy to tumor areas.

STRATIFICATION BY: Participating institutions, disease stage (III or IV).

SPECIAL STUDY PARAMETERS: Urinalysis for VMA and HMA, skin tests with recall antigens (Varidase, mumps, Candida and PPD).

END POINTS: Response/remission rate, objective tumor response, survival rate, quality and length of survival, immunocompetence.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: VCR - 1.5 mg/sqm iv single dose on days 1 and 8 of each 4-week course; CTX - 500 mg/sqm iv on days 1, 57 and q 2 months given at 1000 mg/sqm iv on days 29, 85 and q 2 months thereafter; ADR - 25 mg/sqm/day iv for 3 days beginning on days 1 and 57 and q 2 months thereafter (maximum total cumulative dose 525 mg/sqm).

Arm II: Chemotherapy as in Arm I, plus immunotherapy MER/BCG - 200 micrograms id in each of 5 sites for a total of 1 mg/day on days 8, 36 and 64 and q 4 weeks thereafter.

Evaluate all patients in Arm I and Arm II by the 5th week. If subjective improvement is noted without objective regression, increase ADR dosage. Maintain non-responders on therapy for a minimum of 8 weeks, then remove patients with increase in tumor size or new metastatic lesions from study. Maintain responders on therapy for 12 to 18 months after remission has occurred, or until prior relapse.

Arm III: 1800 to 4000 rads supervoltage radiotherapy given over a period of 5 weeks.

Follow up and evaluate all patients monthly for 6 months, then q 3 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 11/75

PATIENT ACCRUAL: 00581078

11.0006 PHASE I-II COMBINATION CHEMOTHERAPY WITH ADR/CACP/VCR/CTX FOR METASTATIC NEUROBLASTOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7875

OBJECTIVES:

I. Delineate the toxicity of the combination of adriamycin/cis-platinum/vincristine/cyclophosphamide in children with metastatic neuroblastoma.

II. Do a preliminary analysis of the therapeutic efficacy prior to consideration of this four-drug combination as a front-line therapy for children with metastatic neuroblastoma.

PROTOCOL ENTRY CRITERIA: Children between one and 21 years of age with biopsy-proven metastatic neuroblastoma (Stage IV). Only patients at Washington University or the University of Oklahoma are eligible for this pilot study. Patients may receive palliative radiotherapy for symptomatic masses, but there must be at least 1 measurable lesion that has not been treated with radiation therapy. Children less than 5 years of age must have a creatinine level less than or equal to 1.0 mg percent; children over 5 years of age must have a creatinine level less than or equal to 1.2 mg percent. BUN should be less than 30 mg percent.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875; Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: BUN, serum creatinine, creatinine clearance, hematologic function tests, x-rays, tumor measurements.

END POINTS: Response rate, objective tumor response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: The trial will continue until 5 patients who have received at least 2 courses are evaluated. If 2 of the 5 patients respond, the study will be proposed as the front-line groupwide study for newly diagnosed Stage IV neuroblastoma.

DOSAGE SCHEDULE:

VCR - 1.5 mg/sqm iv push on day 1 (maximum dose 1.5 mg); CTX - 500 mg/sqm iv infusion on days 2 and 3, with adequate hydration; ADR - 50 mg/sqm iv push on day 30; CACP - 50 mg/sqm iv over a period of 8 hours on day 30. CACP is given after the administration of 0.5 mg/kg Lasix iv push. Following CACP administration, 1.5 mg/kg Lasix is given. Course is repeated q 42 days. Patients with progressive disease or no evidence of response after 2 courses go off study. Responders will continue treatment for 2 years (maintenance). Patients who develop unacceptable toxicity (cardiac or serum creatinine toxicity) go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; VCR - 1 and 5 mg vials; CTX - 25 and 50 mg tablets and 100, 200, and 500 mg vials.

DATE SUMMARIZED: 12/80

11.0007 COMBINATION CHEMOTHERAPY WITH ADR/CTX/CACP/VCR FOR PEDIATRIC METASTATIC STAGE IV NEUROBLASTOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-8002

OBJECTIVES:

I. Delineate the toxicity of the combination of cyclophosphamide (CTX), vincristine (VCR), adriamycin (ADR), and cis-diamminedichloroplatinum (CACP) in children with metastatic neuroblastoma

II. Do (in patients evaluable for toxicity of this combination) a preliminary analysis of the therapeutic efficacy prior to consideration of this four-drug combination as front-line therapy for children with metastatic neuroblastoma.

PROTOCOL ENTRY CRITERIA: Children from one to 21 years of age with biopsy-proven metastatic neuroblastoma (Stage IV) who have not had prior exposure to cis-platinum. Patients can receive palliative radiation therapy for symptomatic masses. There must be at least 1 measurable lesion (preferably soft tissue mass) that has not been treated with radiation therapy and that will not receive radiation therapy during study. In children less than 5 years of age, the creatinine level should be less than 1.0 mg percent, whereas, in children older than 5 years, the creatinine level should be less than or equal to 1.2 mg percent. BUN should be less than 30 mg percent.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Echocardiogram; EKG; hematologic, renal and hepatic function tests; tumor measurements.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: A minimum of 25 patients will be entered.

DOSAGE SCHEDULE:

Induction: VCR - 1.5 mg/sqm iv on days 1 and 43; CTX - 500 mg/sqm iv on days 2 and 3, 44 and 45; ADR - 30 mg/sqm iv on days 21, 22 and 23; CACP - 90 mg/sqm iv on day 63. Repeat course every 84 days. Patients showing no response after 1 course or progressive disease after 6 weeks go off study. For responders, treatment is continued for 2 years for Maintenance.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 mg vials; CACP - 10 and 25 mg vials; VCR - 1 and 5 mg vials; CTX - 25 and 50 mg tablets or 100, 200 and 500 mg vials.

DATE SUMMARIZED: 06/80

11.0008 SURGERY, CHEMOTHERAPY AND RADIOTHERAPY WITH MAINTENANCE IMMUNOTHERAPY FOR NEUROBLASTOMA

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Tennessee, 38101, United States of America
PROTOCOL NUMBER(S) SJCRH-NB-2; SJCRH-NB-77

OBJECTIVES:

I. Determine whether a larger dose of adriamycin given during induction will increase the remission rate for children with disseminated disease and prolong that remission.

II. Evaluate immunotherapy as maintenance therapy.

III. Evaluate the effect of pulse induction chemotherapy during clinical remission on the duration of disease-free interval.

IV. Determine whether VM-26 in combination with adriamycin with or without cyclophosphamide will induce remission in patients who clinically are partially or completely resistant to the latter two agents.

V. Evaluate in patients with bone marrow tumor the cell kinetic changes induced by VM-26 and adriamycin, and correlate changes in labeling and mitotic indices with clinical responses.

PROTOCOL ENTRY CRITERIA: Patients with neuroblastoma or ganglioneuroblastoma who have had no prior chemotherapy or radiotherapy.

PROTOCOL OUTLINE: Randomized study. Enter patients as follows: Stage I patients to Arm I; Stage IIA patients to Arm II; Stage IIB patients to Arm III; Stage III patients to Arm IV. Randomize Stage III patients under 1 year of age who obtain complete remission on Arm IV to either Arm V or VI; enter those over age 1 to Arm VI. Reassign patients who evidence a partial response in Arm IV to Arm VII. Reassign patients who show no response in Arm IV to Arm VIII.

Arm I: Surgery. Complete surgical resection.

Arm II: Surgery plus Radiotherapy. Surgery as in Arm I plus Radiotherapy to tumor bed.

Arm III: Surgery plus 2-Drug Combination Chemotherapy plus Radiotherapy. Biopsy or subtotal resection; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; plus Radiotherapy to tumor bed and/or lymph nodes.

Arm IV: Surgery plus 2-Drug Combination Chemotherapy. Biopsy, partial or complete resection; CTX, ADR.

Arm V: Immunotherapy. BCG-Glaxo, BCG; plus irradiated tumor cells.

Arm VI: Immunotherapy plus 2-Drug Combination Chemotherapy. BCG plus irradiated tumor cells; CTX, ADR.

Arm VII: 3-Drug Combination Chemotherapy. CTX; ADR; VM-26, NSC-122819.

Arm VIII: 2-Drug Combination Chemotherapy. ADR; VM-26.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: IVP, liver and bone scans, bone survey, coagulation screen, skin tests for recall antigens, in vitro lymphocyte reactions, humoral immunity studies.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 40-50 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: Complete surgical resection.

Arm II: Radiotherapy - 1500-3000 rads, schedule based on age of patient, size of lesion and if prior radiotherapy received.

Arm III: Begin on 4th post-operative day: CTX - 150 mg/sqm/day for 7 days (first course iv, subsequent courses po); ADR - 25 mg/sqm (total cumulative dose 470 mg/sqm) iv on day 8. Repeat cycles q 21 days for 4 months, then resect residual tumor. Initiate 'second look' surgery if indicated. Then administer Radiotherapy - 1000-4000 rads. Maintain patients on 8 additional months of same Chemotherapy regimen.

Arm IV: CTX - as in Arm III; ADR - 45 mg/sqm iv on day 8. Repeat q 21 days for 4 months. Perform 'second look' surgery for removal of residual primary (or biopsy) and clipping plus 1000-4000 rads of radiotherapy for unresectable tumors) for patients who evidence a complete response. For maintenance, randomize complete responders under age 1 to Arm V or VI; cross over patients who evidence complete response over the age of 1 to Arm VI. Cross over partial responders to Arm VII, patients with no response to Arm VIII.

Arm V: BCG - 0.1 ml plus 5 to 10 times 10 to the sixth mixed with 5 to 10 times 10 to the sixth irradiated tumor cells ic once a week for 6 weeks to rotating sites on the upper extremities. The rest 3 months followed by Immunotherapy booster q 2 weeks for 3 courses.

Arm VI: BCG - as in Arm V. CTX; ADR - as in Arm for 4 cycles. Then rest 4 weeks followed by Immunotherapy booster q 2 weeks for 3 courses.

Arm VII: CTX - 150 mg/sqm/day po for 7 days; VM-26 - 75 mg/sqm iv on day 4; ADR - 25 mg/sqm iv 24 hours following VM-26. Repeat cycles q 21 days for 4 cycles. If complete remission obtained, maintain on Arm VI, or if patient under age 1, randomize for Maintenance to either Arm V or VI, and utilize further Surgery and Radiotherapy as for those who showed a complete response initially to Arm IV. For patients failing to achieve a complete response, utilize Surgery and Radiotherapy, as indicated, for residual disease.

Arm VIII: VM-26 - 75 mg/sqm iv; ADR - 25 mg/sqm iv 24 hours following VM-26. Repeat cycles q 14-21 days as tolerated. If complete remission is obtained, continue Chemotherapy for 6 cycles and consider for Surgery and Radiotherapy if indicated. Maintain complete responders on Arm VI. For those who fail to respond, continue Chemotherapy until disease progression or until a maximum ADR dose of 470 mg/sqm has been given.

Dosage modifications for infants and for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/78

11.0009 SURGERY AND CHEMOTHERAPY WITH CTX, ADR, CACP, AND VM-26 FOR NEUROBLASTOMA

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PROTOCOL NUMBER(S) SJCRH-NB-79

OBJECTIVES:

I. Evaluate chemotherapy with cyclophosphamide, adriamycin, VM-26, and cis-platinum as a means of inducing complete remission in children with unresectable or metastatic neuroblastoma and evaluate the disease-free survival time in these patients.

PROTOCOL ENTRY CRITERIA: Previously untreated children with neuroblastoma.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with nonmetastatic surgically unresected disease and negative nodes to Regimen A. Enter patients under the age of 1 year with metastatic disease to Regimen A and those over the age of 1 year with metastatic disease to Regimen B.

Regimen A: 2-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

Regimen B: 4-Drug Combination Chemotherapy. CTX; ADR; cis-Platinum, CACP, NSC-119875; VM-26, NSC-122819.

STRATIFICATION BY: Age (less than 1 year vs. 1 year or more), stage of disease (metastases vs. no metastases).

SPECIAL STUDY PARAMETERS: Surgical documentation of clinical remission.

END POINTS: Complete remission, duration of remission.

CURRENT STATUS: 47 patients were entered as of September 1980.

DOSAGE SCHEDULE: Not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 12/80

11C. RHABDOMYOSARCOMA

11.0010 PRE- VS POSTOPERATIVE CHEMOTHERAPY FOR STAGES I-II RHABDOMYOSARCOMA AND INTENSIVE ESCALATING PREOPERATIVE CHEMOTHERAPY FOR STAGE III DISEASE

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PROTOCOL NUMBER(S) NCI-76-C-385; NCI-POB-764

OBJECTIVES:

I. Determine whether early chemotherapy with VAC (vincristine/actinomycin-D/cyclophosphamide) can reduce the surgical requirements of patients with Stages I-II rhabdomyosarcoma compared to primary surgery.

II. Determine the efficacy of intensive escalating chemotherapy with alternating VAC and VADRC (vincristine/adriamycin/cyclophosphamide) for enhancing survival of patients with Stage III disease.

III. Study the kinetics, biochemistry, immunology, and etiology of childhood rhabdomyosarcoma.

PROTOCOL ENTRY CRITERIA: Patients not over 25 years old with rhabdomyosarcoma or undifferentiated sarcoma who have not had prior surgical debulking, radiotherapy, or chemotherapy.

PROTOCOL OUTLINE: Randomized study. Randomize Stage I-II patients to Arms I and II. Those patients requiring amputations and extensive exenterative procedures are nonrandomly assigned to Arm II. Randomize Stage III patients to Arms III and IV.

Induction:

Arm I: Surgery plus 3-Drug Combination Chemotherapy plus Radiotherapy. VAC: Vincristine, VCR, NSC-67574; Actinomycin-D, ACT-D, NSC-3053; Cyclophosphamide, CTX, NSC-26271.

Arm II: 3-Drug Combination Chemotherapy plus Radiotherapy plus Surgery. VAC.

Arm III: Alternating 3-Drug Combination Chemotherapy plus Immunotherapy plus Surgery. VAC alternating with VADRC: VCR; Adriamycin, ADR, NSC-123127; CTX. Bone marrow storage.

Arm IV: Intensive Alternating 3-Drug Combination Chemotherapy plus Immunotherapy plus Surgery. VAC alternating with VADRC. Bone marrow storage.

Maintenance:

Arm V: 3-Drug Combination Chemotherapy. VAC. Responders from Arms I and II.

Arm VI: Alternating 3-Drug Combination Chemotherapy. VAC alternating with VADRC. Responders from Arms III and IV.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hemogram, blood chemistries, coagulation profile, urinalysis, chest x-ray, whole lung tomograms, gallium scan, bone scan, bone marrow aspirate and biopsy, lumbar puncture, EKG, immune evaluation.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Surgery - operation designed to remove all gross and microscopic tumor consistent with preservation of function. VAC: VCR - 2 mg/sqm (maximum 2 mg) iv on day 1; ACT-D - 2 mg/sqm iv on day 1; CTX - 45 mg/kg iv on day 2. Repeat q 3 weeks for a total of 4 courses. Begin within 10 days of surgery. Radiotherapy - 6000 rads total tumor dose to the total tumor area, with the first 3000 rads being given prior to the first course of Chemotherapy and the second 3000 rads prior to the second course of Chemotherapy, using a shrinking-field technique.

Arm II: Chemotherapy as in Arm I but as initial therapy; Radiotherapy as in Arm I; Surgery as in Arm I, but performed after hematologic recovery from the third course of Chemotherapy. Patients with progressive disease after 2 courses of Chemotherapy will be declared failures of this arm and undergo surgery and subsequent treatment described under Arm I.

Arm III: VAC as in Arm I alternating at 21-day intervals with VADRC: VCR - 2 mg/sqm (maximum 2 mg) iv on day 1; ADR - 60 mg/sqm iv on day 1; CTX - 45 mg/kg iv on day 2. Give a total of 4 courses (2 each of VAC and VADRC). Patients with tumor-free marrow should undergo marrow storage after recovery from the first course. Patients whose bone marrow contained rhabdomyoblasts initially but who become free of marrow involvement after the second or third course will have marrow storage at that time. Surgery - excision of remaining tumor between third and fourth courses of Chemotherapy. Radiotherapy - as in Arm I.

Arm IV: Four alternating courses of VAC and VADRC as in Arm III but at 35-day intervals and escalating CTX as follows: CTX on day 2 in first course, days 2 and 3 in second, days 2, 3, and 4 in third, and days 2, 3, 4, and 5 in fourth. Patients with tumor-free marrows will undergo marrow storage after recovery from the first course. Patients who become tumor-free in marrow after second or third course will have marrow storage performed at that time. Patients with stored marrow will undergo autologous marrow infusion after the fourth course. Surgery - removal of remaining bulk disease at primary and metastatic sites after recovery from the third course of Chemotherapy. Radiotherapy as in Arm I.

CR and PR from Arms I and II begin Maintenance on Arm V; those from Arms III and IV enter Arm VI. Patients from Arms I, II, and III with progressive disease, no response, or relapse enter Arm IV beginning with the second course (first course of VADRC). Patients from Arm IV who have no response or develop relapse and have progressive disease will be considered protocol failures and go off study.

Arm V: VAC: VCR - 2 mg/sqm (maximum 2 mg) iv on day 1; ACT-D - 2 mg/sqm iv on day 1; CTX - 35 mg/kg iv on day 2. Repeat monthly for a total of 2 years, including Induction.

Arm VI: VAC as in Arm V, alternating monthly with VADRC: VCR - 2 mg/sqm (maximum 2 mg) on day 1; ADR - 35 mg/sqm iv on day 1; CTX - 35 mg/kg iv on day 2. Continue for a total of 2 years, including Induction. After a lifetime dose of 500 mg/sqm of ADR has been reached, discontinue ADR and substitute ACT-D.

Progression of disease at any time constitutes relapse. Patients in CR and PR after 1 year and with disease amenable to surgery will undergo surgical extirpation at this time.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

11.0011 SURGERY, RADIOTHERAPY AND COMBINATION CHEMOTHERAPY WITH CTX/ADR/VCR/ACT-D FOR CHILDHOOD RHABDOMYOSARCOMA

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PROTOCOL NUMBER(S) SJCRH-RMS-3

OBJECTIVES:

I. Provide optimal multi-modal therapy for patients with rhabdomyosarcoma utilizing cyclophosphamide (CTX), adriamycin (ADR), vincristine (VCR), and actinomycin-D (ACT-D) in conjunction with surgery and radiotherapy, in an attempt to improve the results of coordinated treatment obtained through the use of the 1968 Rhabdomyosarcoma Protocol and the Rhabdomyosarcoma II Protocol (1973).

II. Determine the sensitivity of rhabdomyosarcoma to combination chemotherapy with CTX/ADR/VCR/ACT-D.

III. Determine the sensitivity of rhabdomyosarcoma to radiation therapy following combination chemotherapy as outlined above.

IV. Reduce the host toxicity of these modalities when administered in combination.

V. Determine the effect of multiple-agent chemotherapy and radiation therapy on in vitro colony formation by bone marrow cells prior to and following therapy with multiple agents and radiation therapy.

PROTOCOL ENTRY CRITERIA: Patients with confirmed tissue diagnosis of rhabdomyosarcoma and no prior chemotherapy or radiotherapy, with careful postsurgical classification, staging of tumors and identification of tumor sites.

PROTOCOL OUTLINE: Nonrandomized study. All patients enter Regimen A. Patients with Stage IIB, IIIA, or IIIB disease are concurrently treated on Regimen B.

Regimen A: 4-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; Actinomycin-D, ACT-D, NSC-3053.

Regimen B: Radiotherapy. Supervoltage to residual tumor areas.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Bone marrow cultures, skin tests, EKG.

END POINTS: Response/remission rate, duration and quality of survival, toxicity/morbidity of treatment, duration of response, objective tumor response.

CURRENT STATUS: About 60 patients will be entered in about 3 years.

DOSAGE SCHEDULE:

Regimen A: CTX - 300 mg/sqm iv on day 1 q 7 days for 2 weeks, then q 14 days to 77 weeks. ADR - 25 mg/sqm (maximum cumulative dose 300 mg/sqm) iv on day 1 for 2 weeks, then q 7 days for 2 doses. Give additional doses in weeks 27, 29, 31, 33, 53, 55, 57 and 59. VCR - 1.5 mg/sqm iv on day 4 for 2 weeks, then, beginning in week 3, q 14 days through week 78. ACT-D - 0.4 mg/sqm iv on day 4 q 7 days for 2 weeks, then, beginning in week 4, q 14 days through week 78.

Regimen B: Enter Stage IIB patients 6 weeks, Stage III patients 5 weeks after beginning of Chemotherapy. 4000-6000 rads given in 5 to 8 weeks to residual tumor or site of biopsy or partial resection. Give reduced dosages to areas of metastases. For Stage IIB include lymph node areas and areas at high risk of involvement; for Stage III dosage and port size will be determined by site and extent of tumor and age of patient.

Follow up all patients indefinitely, all responders after 78 weeks of therapy at least q 3 months for 1.5 years, less frequently thereafter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/78

11D. EWING'S SARCOMA

11.0012 VCR, CTX, ADR, ACT-D CHEMOTHERAPY AND/OR RADIOTHERAPY AND/OR SURGERY FOR PRIMARY LOCALIZED EWING'S SARCOMA OF PELVIC AND SACRAL BONES

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PROTOCOL NUMBER(S) SWOG-7895

OBJECTIVES:

I. Improve the survival of patients with localized Ewing's sarcoma of the pelvis and sacrum who have no evidence of metastases by using an intensive multimodal therapeutic approach.

II. Determine the effectiveness of high-dose intermittent chemotherapy to prevent local recurrence of disease and/or metastases.

III. Determine the effectiveness of surgical resection to control local disease.

IV. Determine the effectiveness of a uniform radiation therapy regimen to control local disease.

V. Identify, determine, and compare the degree of early and late toxicity and sequelae of therapy.

VI. Evaluate and confirm the prognostic characteristics with respect to the tumor and the host.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with biopsy proven localized Ewing's sarcoma of the pelvis or sacrum with verified bone involvement. Patients must be within 1 month of diagnostic biopsy and may have regional lymph node extension of disease.

PROTOCOL OUTLINE: Nonrandomized study. All patients enter Regimen A. Following Regimen A, patients are evaluated for Surgery. Eligible patients enter Regimen B and proceed to Regimen C. Ineligible patients enter Regimen C.

Regimen A: 3-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Regimen B: Surgery plus Single-agent Chemotherapy. VCR.

Regimen C: Radiotherapy plus 2-Drug Combination Chemotherapy followed by 3-Drug Combination Chemotherapy. Supervoltage radiation, plus VCR, ADR, followed by VCR, ADR, CTX, as in Regimen A, with substitution of Actinomycin D for ADR after 4 courses. Actinomycin D, ACT-D, NSC-5053.

STRATIFICATION BY: Participating institutions; sex; surgery status: biopsy vs. incomplete vs. complete resection.

SPECIAL STUDY PARAMETERS: CAT scans or tomograms of chest, CAT scan of primary, bone scan, EKG or echocardiogram.

END POINTS: Disease-free interval, toxicity/morbidity of treatment, response/remission rate, survival time.

CURRENT STATUS: 50 patients will be entered in about 3 to 4 years.

DOSAGE SCHEDULE:

Regimen A: Enter patients as soon as possible after diagnosis and not more than 4 weeks thereafter. VCR - 1.5 mg/sqm (maximum dose 2 mg) iv on days 1 and 22; ADR - 75 mg/sqm iv on day 2; CTX - 1400 mg/sqm iv on day 23.

Regimen B: Surgery. If elected, perform on or about day 42, followed by VCR - 1.5 mg/sqm iv on days 45 and 52.

Regimen C: Radiotherapy. Begin on day 42 for patients not entered to Surgery or within 4 weeks following Surgery. Omit if tumor has been completely excised and there is no evidence of residual disease. Give 4500 rad to entire body hemipelvis and/or sacrum including all soft tissue extensions present at diagnosis, plus a 500-rad boost to the area of tumor extent over a period of 6 weeks. Chemotherapy. If postsurgical, begin 3 days after start of Radiotherapy. If no prior Surgery, begin concomitantly with Radiotherapy. VCR - 1.5 mg/sqm iv on day 1; ADR - 75 mg/sqm iv on day 2. On day 22, resume VCR, ADR, CTX as in Regimen A, given q 6 weeks for 4 courses, followed by VCR, CTX as in Regimen A, omitting ADR and substituting ACT-D - 0.45 mg/sqm/day (maximum dose 0.5 mg) iv on days 1 through 5 of each course. Repeat VCR, CTX, ACT-D q 6 weeks for a total of 7 courses, then discontinue therapy.

Follow up all patients before beginning ACT-D therapy, at end of Chemotherapy and 6 months thereafter, 3 years after study entry and/or at time of relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; ADR - 10 mg vials; CTX - 100, 200, and 500 mg vials; ACT-D - 0.5 mg vials.

DATE SUMMARIZED: 06/79

11.0013 PHASE III COMBINATION CHEMOTHERAPY PLUS RADIOTHERAPY AND SURGERY FOR METASTATIC EWING'S SARCOMA

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PROTOCOL NUMBER(S) SWOG-8095

OBJECTIVES:

I. Determine whether a regimen of surgery (if feasible), chemotherapy with adriamycin (ADR), vincristine (VCR), cyclophosphamide (CTX), 5-fluorouracil (5-FU) and actinomycin-D (ACT-D) plus radiotherapy can improve response, disease-free survival and overall survival of patients with metastatic Ewing's sarcoma.

II. Document and determine the extent of acute and long-term effects of this regimen.

PROTOCOL ENTRY CRITERIA: Newly diagnosed patients of any age with biopsy-proven Ewing's sarcoma with metastatic disease. Patients with malignant cells in the ascites and spinal fluid and those with pleural fluid are eligible. Patients must not have had prior chemotherapy or radiotherapy. Renal and hepatic functions must be adequate (BUN less than 21 mg/dl; bilirubin less than 2 mg/dl, SGOT/PT not increased by more than 25 percent).

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Surgery (if indicated) plus 4-Drug Combination Chemotherapy. Excision of tumor (if indicated); plus Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893.

Regimen B: 3-Drug Combination Chemotherapy, plus Radiotherapy, plus Surgery (if indicated). VCR; CTX; 5-FU; plus supervoltage radiation (Co-60 or higher energy); plus Surgery (if indicated).

Regimen C: Sequential 4-Drug Combination Chemotherapy. VCR; CTX; 5-FU; ADR (replaced, if radiation therapy portals involved the heart, by Actinomycin-D, ACT-D, NSC-3053) followed by VCR; CTX; 5-FU; ACT-D.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: LDH/ESR, bone marrow biopsy, CAT scan or tomogram, bone scan, EKG or echocardiogram, hematologic function tests.

END POINTS: Response/remission rate, duration of response, recurrence rate, disease-free interval, length of survival.

CURRENT STATUS: 63 patients will be entered over approximately 2 years.

DOSAGE SCHEDULE:

Regimen A: Surgical resection (in general, for patients with nonmetastatic disease); VCR - 1.5 mg/sqm iv (maximum dose 2 mg) on days 1, 22, 29, 36 and 43; ADR - 75 mg/sqm iv on days 2 and 44; CTX - 500 mg/sqm iv on days 23, 30 and 37; 5-FU - 300 mg/sqm iv on days 23, 30 and 37. Treatment is followed by a 3-week rest period; the entire course comprises 10 weeks.

Regimen B: Beginning week 11, VCR - 1.5 mg/sqm iv on days 1, 8, 15 and 22; CTX - 500 mg/sqm iv on days 2, 9, 16 and 23; 5-FU - 300 mg/sqm iv on days 2, 9, 16 and 23; after a 2-week rest, initiate Radiotherapy - 4500 rads over a 4- to 5-week period (treatment delivered 5 days per week at 900-1000 rad per week) to the primary lesion; plus irradiation of sites of metastatic disease (dose, schedule and boost depends on site; details are given in the protocol). Surgical excision of expendable bones is performed where indicated.

Regimen C: Beginning week 17, VCR - 1.5 mg/sqm iv on days 1, 22, 29, 36, and 43; ADR - 75 mg/sqm iv on day 2 (if radiation therapy portals involve the heart, ACT-D - 2 mg/sqm is substituted for ADR when the total ADR dose has reached 300 mg/sqm); CTX - 500 mg/sqm iv on days 23, 30, 37, and 44; 5-FU - 300 mg/sqm iv on days 23, 30, 37, and 44. Chemotherapy is followed by a 2-week rest period. Two cycles are given. Beginning week 35, VCR - 1.5 mg/sqm iv on days 1, 22, 29, 36, and 43; ACT-D - 2 mg/sqm iv on day 2; CTX - 500 mg/sqm iv on days 23, 30, 37, 44; 5-FU - 300 mg/sqm iv on days 23, 30, 37 and 44. After waiting 2 weeks for bone marrow recovery, repeat the therapy beginning week 35 for a total of 6 cycles. Regimen C therapy ends on week 109.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CTX - 100, 200 and 500 mg vials; 5-FU - 500 mg ampules; ADR - 10 and 50 mg vials; ACT-D - 0.5 mg vials.

DATE SUMMARIZED: 01/81

11.0014 PROPHYLACTIC PULMONARY IRRADIATION PLUS PRIMARY SITE IRRADIATION AND VAC/VADRC COMBINATION CHEMOTHERAPY FOR LOW-RISK EWING'S SARCOMA

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PROTOCOL NUMBER(S) NCI-77-C-150; NCI-POB-7706

OBJECTIVES:

I. Evaluate the efficacy of prophylactic pulmonary irradiation in conjunction with primary site irradiation and combination chemotherapy with VAC (vincristine/actinomycin-D/cyclophosphamide) and VADRC (vincristine/adriamycin/cyclophosphamide) in the treatment of low-risk Ewing's sarcoma.

II. Evaluate the immunologic status and competence of patients with Ewing's sarcoma as a function of time.

PROTOCOL ENTRY CRITERIA: Patients with a pathologically proven diagnosis of Ewing's sarcoma presenting with distal primary lesions not in the pelvis or spine, without evidence of metastatic disease. Patients may not have received prior chemotherapy or radiation therapy but may have had prior surgical resections.

PROTOCOL OUTLINE: Nonrandomized study.

Initial Therapy.

Regimen A: 3-Drug Combination Chemotherapy. VAC: Vincristine, VCR, NSC-67574; Actinomycin-D, ACT-D, NSC-3053; Cyclophosphamide, CTX, NSC-26271.

Regimen B: Radiotherapy. Radiation to primary site.

Regimen C: Radiotherapy. Prophylactic pulmonary irradiation.

Maintenance.

Regimen D: 3-Drug Combination Chemotherapy. VADRC: VCR; Adriamycin, ADR, NSC-123127; CTX.

STRATIFICATION BY: Site of primary disease (ribs and sternum vs. humerus and femur vs. legs, forearms, hands, and feet vs. skull, scapula, and soft tissue); presenting serum chemistries, particularly LDH. (Stratification omitted, June 1980.)

SPECIAL STUDY PARAMETERS: Hemogram, bone scan, chest and involved bone x-rays, kidney and liver function tests, EKG.

END POINTS: Response/remission rate, disease-free interval, duration of response, objective tumor response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: An accrual of 30 patients is anticipated.

DOSAGE SCHEDULE:

Regimen A: VAC: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ACT-D - 2 mg/sqm iv push on day 1; CTX - 40 mg/kg iv infusion over 30 minutes on day 1 with adequate pre- and posthydration.

Regimen B: 5000 rads over 5 weeks in 200-rad fractions, 5 fractions/week, treating the entire bone wherever possible.

Regimen C: 1500 rads over 2 weeks in ten 150-rad fractions, with shielding of the heart and mediastinum.

Regimen D: VADRC: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ADR - 35 mg/sqm iv push on day 1; CTX - 40 mg/kg iv infusion over 30 minutes on day 1 with adequate hydration before and after medication.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; ACT-D - 500 mg vials.

DATE SUMMARIZED: 08/80

11.0015 TBI PLUS CHEMOTHERAPY WITH VADRC (VCR/ADR/CTX) AND HIGH DOSE VCR/ADR/CTX/DTIC FOR METASTATIC AND HIGH RISK EWING'S SARCOMA

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PROTOCOL NUMBER(S) NCI-77-C-165; NCI-POB-7705

OBJECTIVES:

I. Evaluate the efficacy of TBI (total body irradiation) in combination with high-dose chemotherapy using vincristine/adriamycin/cyclophosphamide/DTIC in the treatment of high risk or metastatic Ewing's sarcoma.

II. Examine the immunological status of patients receiving TBI as a function of time.

III. Determine the utility of autologous marrow infusion in patients receiving high-dose chemotherapy who do not have marrow disease at presentation but who may have metastatic disease in other sites.

PROTOCOL ENTRY CRITERIA: Patients with pathologically proven Ewing's sarcoma presenting with metastatic disease or with pelvic or vertebral primary lesions not previously treated with radiotherapy or chemotherapy. Patients may have had excisional, incisional, or subtotal biopsies of the primary lesion.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients who are candidates for resective surgery to Regimen A and all others to Regimen B; all patients receive Regimen C and Regimen D.

Initial Therapy.

Regimen A: Surgery.

Regimen B: 3-Drug Combination Chemotherapy plus Radiotherapy. VADRC: Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271. Total body irradiation.

Regimen C: 4-Drug High-Dose Combination Chemotherapy plus Immunotherapy. VCR; ADR; CTX; DTIC, NSC-45388. Autologous bone marrow infusion.

Maintenance.

Regimen D: 4-Drug Combination Chemotherapy. VCR; ADR; CTX; DTIC.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hemogram, bone scans, chest x-rays, x-rays of involved bones, kidney and liver function tests, EKG, pulmonary function tests.

END POINTS: Response/remission rate, duration of response, immunologic status, toxicity/morbidity of treatment.

CURRENT STATUS: About 27 new patients will be compared to about 40 historical controls.

DOSAGE SCHEDULE:

Regimen A: Surgical resection of primary lesions and/or metastatic lesions as appropriate.

Regimen B: VADRC: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ADR - 35 mg/sqm iv on day 1; CTX - 40 mg/kg iv over 50 minutes on day 1. Repeat on day 28. Radiotherapy - 5000 rads over 5 weeks in five 200-rad fractions each week to primary lesions, treating the entire involved bone; 4000-5000 rads over 4-5 weeks in twenty to twenty-five 200-rad fractions to metastatic areas, as tolerated; a total of 150 rads total body irradiation over 5 weeks in two 15-rad doses per week beginning the week subsequent to primary irradiation.

Regimen C: Administer following total body irradiation. VCR - 2 mg/sqm (maximum 2 mg) iv push on days 1 and 7; ADR - 35 mg/sqm iv push on days 1 and 2; CTX - 40 mg/kg iv over 30 minutes on days 1 and 2; DTIC - 250 mg/sqm iv over 30 minutes on days 1, 2, and 3. Autologous bone marrow infusion, when performed, to be carried out 24 hours subsequent to the completion of high-dose Chemotherapy.

Regimen D: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ADR - 35 mg/sqm iv push on day 1; CTX - 40 mg/kg iv over 30 minutes on day 1; DTIC - 250 mg/sqm iv over 30 minutes on days 1 and 2. Repeat q 6 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; DTIC - 100 and 200 mg vials.

DATE SUMMARIZED: 08/80

11.0016 HIGH-DOSE CHEMOTHERAPY WITH VAC (VCR/ACT-D/CTX) PLUS DTIC OR VADRC (VCR/ADR/CTX) PLUS DTIC FOR RECURRENT EWING'S SARCOMA

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PROTOCOL NUMBER(S) NCI-77-C-167

OBJECTIVES:

I. Evaluate the role of high-dose chemotherapy with vincristine/actinomycin-D/cyclophosphamide/DTIC or vincristine/adriamycin/cyclophosphamide/DTIC in prolonging the disease-free interval of patients with recurrent Ewing's sarcoma, using historical controls from the same institution.

II. Serially evaluate the immunologic status of patients receiving high-dose chemotherapy without total body irradiation.

PROTOCOL ENTRY CRITERIA: Patients previously treated at the National Cancer Institute who have a documented relapse of Ewing's sarcoma either in the primary site or elsewhere. Patients with a history of pulmonary or whole brain irradiation of more than 2000 rads will be considered individually. Patients may not have a history of hemorrhagic cystitis.

PROTOCOL OUTLINE: Randomized study. Enter on Regimen A those patients who have received no more than 380 mg/sqm total cumulative dose of ADR, those with no more than 300 mg/sqm adriamycin plus at least 3000 rads to the mediastinum, and those who have not had adriamycin discontinued because of cardiac compromise. Randomize following initial therapy in Regimen A. Enter patients ineligible for Regimen A to Regimen B.

Regimen A:

Initial Therapy: 3-Drug Combination Chemotherapy plus Radiotherapy. VADRC: Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

Arm I: 4-Drug Combination High-Dose Pulse Chemotherapy. VCR; ADR; CTX; DTIC, NSC-45388.

Arm II: 4-Drug Combination Frequent-Dose Pulse Chemotherapy. VCR; ADR; CTX; DTIC.

Maintenance: 3-Drug Combination Chemotherapy. VADRC.

Regimen B:

Initial Therapy: 3-Drug Combination Chemotherapy plus Radiotherapy. VAC. VCR; Actinomycin-D, ACT-D, NSC-3053; CTX.

4-Drug Combination High-Dose Chemotherapy. VCR; ACT-D, CTX; DTIC.

Maintenance: 3-Drug Combination Chemotherapy. VAC.

STRATIFICATION BY: Lifetime cumulative dose of ADR (more or less than 380 mg/sqm in patients without significant mediastinal irradiation, more or less than 300 mg/sqm in patients with at least 3000 rads mediastinal irradiation).

SPECIAL STUDY PARAMETERS: Hemogram, bone scan, x-rays of chest and involved bones, liver and kidney function tests, EKG.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 26 new patients will be compared with at least 30 historical controls.

DOSAGE SCHEDULE:

Regimen A:

Initial Therapy: VADRC: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ADR - 35 mg/sqm iv push on day 1; CTX - 40 mg/kg iv on day 1. Repeat on day 28. Radiotherapy - 5000 rads to known lesions in 200 rad fractions over 5 weeks, treating 5 days per week. Patients with progressive disease after completing Radiotherapy go off study.

Arm I: Begin therapy on week 7 after initiation of treatment. VCR - 2 mg/sqm (maximum 2 mg) iv push on days 1 and 7; ADR - 35 mg/sqm iv push on days 1, 2, and 3; CTX - 40 mg/kg iv on days 1, 2, and 3; DTIC - 250 mg/sqm iv on days 1 through 5. Begin Maintenance on week 16.

Arm II: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ADR - 35 mg/sqm iv push on day 1; CTX - 40 mg/kg iv on day 1; DTIC - 250 mg/sqm iv on days 1 and 2. Repeat weekly for a total of 3 courses but omit DTIC from the last course. Begin Maintenance on week 16.

Maintenance: VADRC: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ADR - 35 mg/sqm iv push on day 1; CTX - 40 mg/kg iv on day 1. Repeat q 4 weeks for a total of 15 cycles.

Regimen B:

Initial Therapy: VAC: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ACT-D - 2 mg/sqm iv push on day 1; CTX - 40 mg/kg iv on day 1. Repeat on day 28. Radiotherapy as in Regimen A. Patients with progressive disease after Radiotherapy go off study.

High-Dose Chemotherapy: Treat at 7 weeks from time of entry on study. VCR - 2 mg/sqm (maximum 2 mg) iv push on days 1 and 7; ACT-D - 2 mg/sqm on day 1; CTX - 40 mg/kg iv on days 1, 2, and 3; DTIC - 250 mg/sqm iv on days 1 through 5. Begin Maintenance on week 14.

Maintenance: VAC: VCR - 2 mg/sqm (maximum 2 mg) iv push on day 1; ACT-D - 2 mg/sqm iv push on day 1; CTX - 40 mg/kg iv on day 1. Repeat q 4 weeks for a total of 15 cycles.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; DTIC - 100 and 200 mg vials; ACT-D - 500 mg vials.

DATE SUMMARIZED: 08/80

11.0017 INDUCTION WITH CTX/ADR, MAINTENANCE WITH VCR/ACT-D/BCNU/CTX/ADR AND DELAYED RADIOTHERAPY FOR EWING'S SARCOMA

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Tennessee, 38101, United States of America
PROTOCOL NUMBER(S) SJCRH-EWI-79

OBJECTIVES:

I. Evaluate the response of Ewing's sarcoma to Induction with cyclophosphamide and adriamycin and Maintenance with vincristine, actinomycin-D, cyclophosphamide, BCNU, and adriamycin.

II. Evaluate local control of tumor by delayed, low-dose, limited-port radiotherapy.

PROTOCOL ENTRY CRITERIA: Previously untreated patients under the age of 25 years with biopsy-proven Ewing's sarcoma.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 2-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

Maintenance: 5-Drug Combination Chemotherapy plus Radiotherapy. Vincristine, VCR, NSC-67574; Actinomycin-D, ACT-D, NSC-3053; BCNU, NSC-409962; CTX; ADR; plus delayed, low-dose, limited-port Radiotherapy.

STRATIFICATION BY: Local vs. metastatic disease.

SPECIAL STUDY PARAMETERS: CT of chest and primary, bone scan, gallium scan, liver scan, appropriate radiographs, bone marrow.

END POINTS: Response/remission rate, disease-free survival.

CURRENT STATUS: 16 patients had been entered as of September 1980.

DOSAGE SCHEDULE: Not given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 01/81

11.0018 PILOT STUDY TREATMENT OF EWING'S TUMOR WITH RADIOTHERAPY, SURGERY, AND CHEMOTHERAPY WITH ACT-D/CTX/VCR/ADR/MTX

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Onco-Hermatologia, Apartado 1654, San Jose, Costa Rica
PROTOCOL NUMBER(S) COSTA-RICA-PE278

OBJECTIVES:

I. Determine whether a combination of surgery, irradiation and chemotherapy with 5 drugs administered sequentially to patients with clinically localized Ewing's tumor can keep them free of the disease long enough to cure them.

II. Compare the survival in remission of our group with that of other groups using surgery, irradiation and different chemotherapy courses.

III. Evaluate the toxicity of the chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients under 12 years of age with histologically diagnosed localized Ewing's tumor, and with no prior radiotherapy or chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with resectable tumor to Regimen A, those with nonresectable tumor to Regimen B.

Regimen A: Surgery plus 5-Drug Combination Chemotherapy plus Radiotherapy. Resection. Actinomycin, ACT-D, NSC-3053; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740. Radiotherapy, total dose 3,000-4,000 rads.

Regimen B: 5-Drug Combination Chemotherapy plus Radiotherapy. ACT-D; CTX; VCR; ADR; MTX. Radiotherapy, total dose 5,000-7,000 rads.

STRATIFICATION BY: Participating institutions, extent of tumor, tumor resectability.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Toxicity/morbidity of treatment, recurrence rate, hematuria, ECG irregularities.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: ACT-D - 15 mg/kg/day for 5 days iv; CTX - 600 mg/sqm iv, day 15; VCR - 1.5 mg/sqm iv, day 15; ADR - 40 mg/sqm iv day 30; MTX - 30 mg/sqm iv, day 30. Radiotherapy - 3,000-4,000 rads over period of 5-6 weeks, following surgery. Chemotherapy repeated 12 times or until appearance of distal metastases.

Regimen B: ACT-D, CTX, VCR, ADR, MTX - all as in Regimen A. Radiotherapy - 5,000-7,000 rads. If metaphysis or epiphysis involved, adjacent bones treated with two-thirds total dose.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

11E. PEDIATRIC SOLID TUMORS—GENERAL

11.0019 PHASE II CHEMOTHERAPY WITH HIGH DOSE HEXAMETHYLMELAMINE FOR RESISTANT CHILDHOOD LYMPHOMAS AND OTHER SOLID TUMORS

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PROTOCOL NUMBER(S) CCG-074

OBJECTIVES:

I. Determine the efficacy and toxicity of chemotherapy with high-dose hexamethylmelamine for Hodgkin's and non-Hodgkin's lymphomas and other solid tumors of childhood resistant to conventional therapy.

PROTOCOL ENTRY CRITERIA: Patients under 21 years of age with histologically confirmed, measurable Hodgkin's and non-Hodgkin's lymphomas or other solid tumors (to be entered at a later date) which are resistant to conventional therapy. Patients must have a life expectancy of at least 4 weeks and adequate liver and kidney function and must not be eligible for higher priority protocols as designated by Associate Chairman, Solid Tumors, nor have had progressive disease, chemotherapy, or radiotherapy in the prior 2 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Hexamethylmelamine, HMM, NSC-13875.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Catecholamines, alpha fetoprotein, CEA.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: As of 08/80, 9 patients have been entered.

DOSAGE SCHEDULE:

HMM - 12 mg/kg/day po in 4 divided doses for 21 days. Repeat course q 31 days. Continue therapy if there is any objective or subjective response. Remove from study patients with progressive disease or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: HMM - 50 mg capsules.

DATE SUMMARIZED: 11/79

11.0020 PHASE II CHEMOTHERAPY WITH ADCONFU (ADR/CTX/VCR/5-FU) PLUS LITHIUM CARBONATE FOR NONRESECTABLE SOLID TUMORS IN CHILDREN

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PROTOCOL NUMBER(S) SWOG-7607B

OBJECTIVES:

I. Determine complete and partial response rates to the combination ADCONFU: adriamycin (ADR), cyclophosphamide (CTX), vincristine (VCR), and 5-fluorouracil (5-FU), plus lithium carbonate in the treatment of solid tumors in previously treated or untreated children and adolescents.

II. Examine duration of remissions in responding patients.

III. Document the toxicity of the combination of these drugs.

IV. Evaluate the efficacy of lithium carbonate in reducing granulocytic myelosuppression following combination chemotherapy of childhood solid tumors.

V. Observe factors predisposing to lithium carbonate toxicity when given in this clinical setting.

VI. Compare results with those obtained with ADCONFU therapy without lithium carbonate (SWOG-7607A).

PROTOCOL ENTRY CRITERIA: Patients less than 21 years of age with measurable nonresectable solid tumors (epithelial or previously treated sarcomas) not eligible for SWOG studies of higher priority. Patients must have had no prior therapy with ADR, CTX, 5-FU, no present therapy with saluretic diuretics nor haloperidol and must have recovered from and be off all prior chemotherapy or radiotherapy for two weeks. Patients must have adequate liver, renal and hematologic function.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy plus Supportive Therapy. Adriamycin, ADR, NSC-123127, or Actinomycin-D, ACT-D, NSC-3053; 5-Fluorouracil, 5-FU, NSC-19893; Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; plus Lithium carbonate, NSC-16985, for alternate courses.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Liver and kidney function tests, red cell and plasma lithium levels, free thyroxine index of T4.

END POINTS: Toxicity/morbidity of treatment, objective tumor response, response/remission rate, duration of response.

CURRENT STATUS: 50 patients will be entered in about 18 months.

DOSAGE SCHEDULE:

Good-risk patients have granulocyte counts above 100,000; poor-risk patients (PRP) have granulocyte counts below 100,000.

ADCONFU: ADR - 45 mg/sqm (30 mg/sqm for PRP) iv on day 1 (total cumulative dose 450 mg/sqm). For patients who have or who now are receiving radiotherapy to mediastimal or pulmonary areas, limit total ADR dose to 350 mg/sqm. When maximum ADR dose has been given, replace ADR with ACT-D - 0.27 mg/sqm iv on days 1 through 5 (days 1, 2, and 3 for PRP); 5-FU - 240 mg/sqm iv on days 1 through 5 (days 1, 2, and 3 for PRP); CTX - 210 mg/sqm on days 1 through 5 (days 1, 2 and 3 for PRP); VCR - 1.5 mg/sqm iv on day 1; Lithium carbonate - 900 mg/sqm/day po in 3 divided doses on days 4 through 19 of alternating ADCONFU courses beginning with first course.

Repeat course q 3 weeks for a minimum of 2 courses delaying next course if indicated by hematologic toxicity. Continue treatment until disease progression or relapse or until toxicity precludes further treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg vials; CTX - 100, 200, and 500 mg vials; VCR - 1 and 5 mg vials; 5-FU - 500 mg ampules; Lithium carbonate - 300 mg capsules; ACT-D - 0.5 mg/vials.

DATE SUMMARIZED: 11/79

PATIENT ACCRUAL: 00050779

11.0021 CHEMOTHERAPY WITH VBL/BLEO FOR METASTATIC SOLID TUMORS IN CHILDREN

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7617; MDAR-170

OBJECTIVES:

I. Determine the response rate of the vinblastine sulfate/ bleomycin combination in children with advanced metastatic solid tumors.

II. Determine the toxicity of this combination in children.

PROTOCOL ENTRY CRITERIA: Previously treated patients with recurrent or metastatic solid tumors (soft tissue and bony sarcomas, Wilms' tumor, neuroblastomas, carcinomas, embryonal carcinomas, teratomas, Hodgkin's and non-Hodgkin's lymphomas. Patients must be 18 years or under at the time of diagnosis and under 21 at the time of entry. Patients must have measurable tumor parameters.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; Vinblastine sulfate, VBL, NSC-49842.

STRATIFICATION BY: Good-risk patients - no history of previous radiation therapy to the lungs or mediastinum and who have a platelet count of more than 150,000 and granulocyte count of more than 2000 at prestudy evaluation. Poor-risk patients - history of previous radiation therapy to the lungs and mediastinum and platelet count of less than 150,000 and granulocyte count of less than 2,000 at prestudy evaluation. Include as poor risk, those patients with bone marrow replacement by tumor cells.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Objective tumor response, response/remission rate, duration of remission, toxicity/morbidity of treatment.

CURRENT STATUS: Enter 10 patients in each tumor category.

DOSAGE SCHEDULE:

Arm I: BLEO - 15 mg/sqm iv on days 2 through 6; VBL - 3 mg/sqm iv push on days 1 and 2. (Patients with history of pulmonary radiotherapy receive BLEO - 7.5 mg/sqm iv on days 2 through 6; patients without history of pulmonary radiotherapy receive 15 mg/sqm iv on days 2 through 6 regardless of platelet and granulocyte counts. Patients with poor-risk hematologic status regardless of history of pulmonary or mediastinal radiation receive VBL - 3 mg/sqm iv push on day 1.) For patients who have undergone pulmonary radiotherapy, total BLEO dose shall not exceed 300 mg/sqm; for others, total BLEO dose shall not exceed 150 mg/sqm. Repeat course q 4 weeks for a minimum of 2 courses until evidence of toxicity or disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 mg vials; VBL - 10 mg vials.

DATE SUMMARIZED: 10/76

PATIENT ACCRUAL: 00310179

11.0022 PHASE II CHEMOTHERAPY WITH RUBIDAZONE FOR SOLID TUMORS IN CHILDREN

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PROTOCOL NUMBER(S) SWOG-7843

OBJECTIVES:

I. Determine the clinical efficacy of rubidazone (RBD) in the treatment of malignant tumors in children with and without previous anthracycline therapy.

II. Determine the toxicity of RBD in children with solid tumors.

PROTOCOL ENTRY CRITERIA: Patients not over 21 years old with measurable solid tumor resistant to conventional chemotherapy. Patients must have adequate cardiac status and any prior therapy with adriamycin must have been less than 200 mg/sqm and with daunomycin less than 300 mg/sqm. One week must have elapsed since prior chemotherapy, 3 weeks since prior radiotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Rubidazone, RBD, NSC-164011.

STRATIFICATION: Participating institutions, disease type, number of previous relapses, previous therapy.

SPECIAL STUDY PARAMETERS: Cardiac function tests, liver spleen and tumor measurements, liver and spleen and CAT scans, ultrasonography.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 15 to 30 patients will be entered in 1 year.

DOSAGE SCHEDULE:

RBD - 175 mg/sqm (from 75 mg/sqm to 225 mg/sqm as tolerated for good risk patients; start poor risk patients with extensive prior radiotherapy or inadequate hematologic or liver function at 150 mg/sqm) iv on day 1. Repeat course q 3 weeks if wbc have returned to at least 3000, platelets to at least 100,000. Remove patients with progressive disease after 2 courses. Evaluate patients after a cumulative dose of 1000 mg/sqm. Patients with no prior adriamycin therapy may receive up to 1400 mg/sqm.

DOSAGE FORMS: RBD - 50 mg vials.

Dosage modifications for toxicity are given.

DATE SUMMARIZED: 10/79

11.0023 PHASE II CHEMOTHERAPY WITH M-AMSA FOR CHILDREN WITH SOLID TUMORS

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PROTOCOL NUMBER(S) SWOG-8018

OBJECTIVES:

I. Determine the clinical efficacy of m-AMSA (AMSA) as indicated by the induction of partial or complete remission in pediatric patients with solid tumors in relapse.

II. Assess the toxicity of m-AMSA in children.

PROTOCOL ENTRY CRITERIA: Patients 21 years of age or younger with measurable solid tumors in relapse who are not eligible for protocols of higher priority and who are resistant to standard forms of therapy. Life expectancy should be at least 4 weeks. Patients must have recovered from prior significant toxicity. AGC must be greater than 1500/cumm and platelet count greater than 100, 000/cumm, unless there is evidence of tumor invasion of the bone marrow. Normal renal and hepatic function and a normal serum potassium level are required. Patients must not have received any prior treatment with m-AMSA. Palliative radiotherapy may be given provided the irradiated tumor is not being evaluated for tumor response.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Echocardiogram, bone marrow aspiration or biopsy, chest x-ray and other radiologic studies to determine the extent of tumor, CBC and platelet counts.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 30 patients will be entered over 2 years.

DOSAGE SCHEDULE:

AMSA - 50 mg/sqm/day iv infusion over 1-2 hours for 5 days. Repeat q 21 days. A minimum of 2 courses is required for an adequate trial. Patients who show no response or intolerable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 10/80

11.0024 PARENTERAL HYPERALIMENTATION AS ADJUVANT TO AGGRESSIVE CHEMOTHERAPY IN RHABDOMYOSARCOMA AND NEUROBLASTOMA

Goodgame, J. T., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America

PROTOCOL NUMBER(S) NCI-76-C-203

OBJECTIVES:

I. Ascertain whether optimal nutrition via parenteral alimentation improves the tolerance of patients with rhabdomyosarcoma and neuroblastoma to aggressive chemotherapy.

II. Determine the influence that nutritional support has on the response of the tumor to aggressive chemotherapy in terms of survival.

III. Determine whether host defenses as measured by in vivo parameters of immune response are changed by maintenance of optimal nutrition.

IV. Determine whether there is a significant aggravation of the management problems of support for these patients as a result of their total parenteral nutrition.

PROTOCOL ENTRY CRITERIA: Patients over the age of 6 years with neuroblastoma or rhabdomyosarcoma. Patients with rhabdomyosarcoma must have Stage III disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: Nutritional Therapy. Dextrose and Freamine.

Arm II: Control.

STRATIFICATION BY: Tumor type (rhabdomyosarcoma vs neuroblastoma).

SPECIAL STUDY PARAMETERS: Nutritional status, hematological status, gastrointestinal toxicity, liver function tests, renal function tests, EKG, chest x-ray, echo cardiogram, electrolyte and amino acid intake and output, serum iron, total iron binding capacity, serum B12, glucagon, growth hormone, serum insulin.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: 25 percent dextrose and 4.25 percent Freamine sufficient to give 40 calories/kg/day and 0.30 g nitrogen/kg ideal weight/day. Begin 3 days prior to and continue for 15 days after Chemotherapy cycles (details of Chemotherapy not given).

Arm II: Observe.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

11.0025 PHASE II TRIAL OF ISOPHOSPHAMIDE IN REFRACTORY PEDIATRIC MALIGNANCIES

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PROTOCOL NUMBER(S) NCI-78-C-140; NCI-POB-7809

OBJECTIVES:

I. Determine the antitumor activity of isophosphamide administered daily for 5 days in children with malignancies who have failed conventional treatment regimens.

II. Determine the effectiveness of isophosphamide in malignancies and diseases no longer responsive to cyclophosphamide.

PROTOCOL ENTRY CRITERIA: All patients with histologic proof of cancer who have failed conventional modes of treatment for their malignancies. Patients must have recovered from the toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy before entry. Patients should have adequate bone marrow, liver, and kidney function and normal metabolic parameters.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Isophosphamide, IPP, NSC-109724.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, electrolytes, chest x-ray, other x-rays as appropriate, EKG, measurement of palpable lesions.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

IPP - 1200 mg/sqm/day by continuous iv infusion for 5 days. Repeat q 2-3 weeks depending on granulocyte and platelet counts. Patients with progressive disease after 2 courses go off study. Responders continue until disease becomes refractory.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: 1 and 2 g vials.

DATE SUMMARIZED: 08/80

11.0026 PHASE II IMMUNOTHERAPY WITH STABILIZED POLY IC IN THE TREATMENT OF REFRACTORY PEDIATRIC SOLID TUMORS

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PROTOCOL NUMBER(S) NCI-79-C-23; NCI-POB-7803

OBJECTIVES:

I. Assess the therapeutic efficacy of stabilized poly IC in patients with pediatric solid tumors who have failed several sequences of Phase III protocols.

PROTOCOL ENTRY CRITERIA: All patients with pediatric solid tumors who are in relapse after having been treated with standard drugs and investigational drugs of higher priority.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Immunotherapy. Poly IC, NSC-120949.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, bone marrow aspiration, serum protein electrophoresis, coagulation studies.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 15 patients for each tumor category will be required.

DOSAGE SCHEDULE:

Induction: Poly IC - 12 mg/sqm/day iv over 60 minutes on days 1 through 14. Repeat q 21 days. Begin Maintenance whtn patient is free of disease or disease is stable or shows partial response. Patients with progressive disease any time after 21 days go off study.

Maintenance: Poly IC - 12 mg/sqm/day iv on days 1 through 7. Repeat q 28 days.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

11.0027 SURGERY COMBINED WITH CTX/MTX/CF/ADR FOR OSTEOSARCOMA IN CHILDREN

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PROTOCOL NUMBER(S) COSTA-RICA-P01179

OBJECTIVES:

I. Establish a set, systematic program for the diagnosis, treatment, monitoring and rehabilitation of children with osteosarcoma.

II. Evaluate the efficacy of surgery for resecting the tumor while preserving the function and aesthetic appearance of the limb.

III. Establish the efficacy of multiple and sequential chemotherapy for prevention and control of metastases.

IV. Determine whether increasing coagulation time with warfarin affects the incidence of metastases in amputations.

PROTOCOL ENTRY CRITERIA: Children with osteosarcoma of the extremity and adequate renal and hepatic function.

PROTOCOL OUTLINE: Nonrandomized study.

Surgery plus 4-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Prior chemotherapy; prior surgery: amputation vs. resection.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, survival rate, survival time, incidence of metastases, disease-free interval.

CURRENT STATUS: 20 patients will be entered.

DOSAGE SCHEDULE:

CTX - 600 mg/sqm iv on day 0 (prior to or during biopsy; MTX - 500 mg/sqm iv on days 15 (following tumor resection or amputation) and 45 and followed on both days by CF - 90 mg/sqm po beginning 8 hours after MTX; ADR - 45 mg/sqm iv on day 30.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/80

SECTION 12

HEAD AND NECK TUMORS

CLB-8001	PILOT COMBINATION CHEMOTHERAPY WITH BLEO/CTX/MTX/5-FU FOR SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK	12.0001
EST-PC-379	PHASE II PILOT CHEMOTHERAPY WITH VINDESINE FOR ADVANCED CANCER OF THE HEAD AND NECK	12.0002
EST-PF-379	PILOT STUDY OF COMBINATION CHEMOTHERAPY USING BLEO/DDP/HU/MTX FOR ADVANCED HEAD AND NECK CANCER	12.0003
EST-2375	PHASE III STUDY OF CHEMOTHERAPY WITH ADRIAMYCIN WITH VS WITHOUT CIS-DIAMMINE-DICHLOROPLATINUM FOR THYROID CARCINOMA	12.0004
EST-2379	PHASE II STUDY OF NEW AGENTS IN TREATMENT OF ADVANCED CANCER OF HEAD AND NECK: MGBG VS PALA	12.0005
NCOG-7H61	PHASE III RADIOTHERAPY ALONE VS COMBINED WITH BLEOMYCIN CHEMOTHERAPY FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK	12.0006
NCOG-7H81	PHASE III CHEMOTHERAPY WITH CACP VS CACP/MTX/CF FOR METASTATIC OR RECURRENT SQUAMOUS CELL CARCINOMA OF THE HEAD & NECK	12.0007
RTOG-7609	NEUTRON RADIOTHERAPY FOR POTENTIALLY OPERABLE PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY, PHARYNX AND LARYNX	12.0008
RTOG-7610	NEUTRON AND/OR PHOTON RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY, PHARYNX AND LARYNX	12.0009
RTOG-7802	PHASE II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS RADIOTHERAPY FOR RECURRENT HEAD AND NECK SQUAMOUS CELL CARCINOMA	12.0010
RTOG-7808	RADIOTHERAPY PLUS NEUTRON VS CONVENTIONAL BOOST FOR SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY, PHARYNX AND LARYNX	12.0011
RTOG-7828	RADIOTHERAPY VS PION RADIOTHERAPY FOR STAGE III OR IV SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY AND PHARYNX	12.0012
RTOG-7904	PHASE I/II MISONIDAZOLE RADIOSENSITIZATION & HIGH FRACTIONAL DOSE RADIOTHERAPY FOR ADVANCED SQUAMOUS CELL HEAD AND NECK CANCER	12.0013
RTOG-7912	LIMITED VS RADICAL NECK DISSECTION PLUS PRE- OR POSTOPERATIVE RADIOTHERAPY FOR HEAD AND NECK CARCINOMA WITH CLINICALLY POSITIVE NODES	12.0014
RTOG-7913	HYPERFRACTIONATED VS CONVENTIONAL RADIOTHERAPY FOR ADVANCED CARCINOMA OF THE ORAL CAVITY, PHARYNX, LARYNX OR SINUSES	12.0015
RTOG-7914	PHASE III ADJUVANT CHEMOTHERAPY WITH CIS-PLATINUM FOR DEFINITIVELY TREATED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK	12.0016
RTOG-7915	PHASE III RADIOTHERAPY WITH OR WITHOUT MISONIDAZOLE FOR LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK	12.0017

SEG-HN-P44 PILOT STUDY OF DIBROMODULCITOL FOR SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK 12.0018
SEG-78THY0102 PHASE II CHEMOTHERAPY WITH ADR/CACP FOR ADVANCED THYROID CANCER 12.0019
SEG-79HN235 PHASE II PVB (CACP/VBL/BLEO) VS MTX FOR RECURRENT OR METASTATIC SQUAMOUS CELL CARCINOMA OF HEAD AND NECK ORIGIN 12.0020
SEG-79HN356 SURGERY & RADIOTHERAPY WITH OR WITHOUT MTX/CF/BLEO/CACP FOR STAGE III OR IV EPIDERMOID CANCER OF THE MOUTH, HYPOPHARYNX, LARYNX 12.0021
SEG-79HN357 MTX/CF/BLEO/CACP AND RADIOTHERAPY WITH OR WITHOUT SURGERY FOR STAGE IV EPIDERMOID CANCER OF THE MOUTH, LARYNX & HYPOPHARYNX 12.0022
SWOG-7902 PHASE III CHEMOTHERAPY WITH COB (CACP/VCR/BLEO) PLUS RADIOTHERAPY AND SURGERY VS RADIOTHERAPY PLUS SURGERY FOR HEAD AND NECK CANCER 12.0023
SWOG-7915 PHASE II CHEMOTHERAPY WITH ADR/CTX/5-FU FOR ADVANCED CARCINOMA OF THE SALIVARY GLAND 12.0024
SWOG-7923 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE FOR METASTATIC OR LOCALLY RECURRENT SQUAMOUS CELL CARCINOMA OF THE HEAD & NECK 12.0025
SWOG-7934 PHASE II CHEMOTHERAPY WITH AMSA FOR METASTATIC SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK 12.0026
SWOG-8006 PHASE III SURGERY & RADIOTHERAPY WITH/WITHOUT PREOPERATIVE BLEO/CACP/MTX/VCR FOR STAGE III/IV EPIDERMOID CARCINOMA OF THE HEAD AND NECK 12.0027
BCRP-8026 COMBINATION CHEMOTHERAPY WITH CTX/CACP FOR ADVANCED, RECURRENT EPIDERMOID CARCINOMA OF THE HEAD AND NECK 12.0028
BCRP-8028 PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE (AZQ) FOR ADVANCED EPIDERMOID CARCINOMA OF THE HEAD AND NECK 12.0029
HNCP-178 ADJUVANT CHEMOTHERAPY WITH CACP/BLEO PLUS SURGERY AND RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK 12.0030
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SECTION 12

HEAD AND NECK TUMORS

12.0001 PILOT COMBINATION CHEMOTHERAPY WITH BLEO/CTX/MTX/5-FU FOR SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) CLB-8001

OBJECTIVES:

I. Determine the response rate, duration of response, survival and tolerance to bleomycin (BLEO)/cyclophosphamide (CTX)/methotrexate (MTX)/5-fluorouracil (5-FU) in Stage III or IV cancer of the head and neck.

II. Determine differences in response based on prior therapy.

III. Determine whether disease previously not amenable to surgery or radiotherapy can be converted to be eligible for those therapies.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven squamous cell carcinoma of the oral cavity, nasopharynx, hypopharynx, tonsil, trachea, and larynx. Patients must have a performance status of 0 to 2, adequate hematologic, pulmonary and renal status, and no prior chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Participating institutions, prior therapy.

SPECIAL STUDY PARAMETERS: Hepatic and renal function.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, duration of response, survival rate.

CURRENT STATUS: 30 to 35 patients to be entered in 3 to 6 months.

DOSAGE SCHEDULE:

BLEO - 7.5 mg/sqm (maximum cumulative dose 225 mg/sqm) continuous iv infusion on days 1 through 3; CTX - 300 mg/sqm iv on day 5; MTX - 30 mg/sqm iv on day 5; 5-FU - 300 mg/sqm iv on day 5. Repeat course q 3 weeks for 10 courses; then continue, omitting BLEO. Repeat until disease progresses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 U ampules; CTX - 500 mg ampules; MTX - 50 mg vials; 5-FU - 500 mg ampules.

DATE SUMMARIZED: 02/80

12.0002 PHASE II PILOT CHEMOTHERAPY WITH VINDESINE FOR ADVANCED CANCER OF THE HEAD AND NECK

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-PC-379

OBJECTIVES:

I. Determine effects of chemotherapy with vindesine for advanced squamous cell cancer of the head and neck.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, graded (well differentiated, moderately differentiated, or poorly differentiated) squamous cell cancer of the head and neck (including lymph epitheliomas) who are not eligible for ECOG protocols of higher priority. Patients must have metastases below the clavicle, or if none, recurrent disease following radiotherapy or radiotherapy plus surgery which is uncontrollable locally by either or both modalities, or residual tumor after at least 5000 rads of radiotherapy if it is histologically confirmed more than 2 months after completion of radiotherapy, measurable, and not amenable to surgical salvage. Patients must have adequate hematologic, liver, and kidney function and an ECOG performance status of at least 3. Patients must not be pregnant or have prior exposure to the protocol drug, and must not have had prior therapy in the past 6 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 30 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 3 mg/sqm iv q 7 days for 28 days. (Care should be taken to avoid paravenous infiltration because ulceration can be expected to result. Addendum 1, October 1979) Follow patients until death. Remove from study patients with progression, toxicity requiring cessation of therapy for more than 6 weeks, or relapse after complete or partial response.

DOSAGE FORMS: DAVA - 50 mg vials.

DATE SUMMARIZED: 11/79

12.0003 PILOT STUDY OF COMBINATION CHEMOTHERAPY USING BLEO/DDP/HU/MTX FOR ADVANCED HEAD AND NECK CANCER

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PROTOCOL NUMBER(S) EST-PF-379

OBJECTIVES:

I. Determine whether a combination of the four agents under study is tolerable from the point of view of toxicity in the generally debilitated group of patients with advanced head and neck carcinoma.

II. Gather preliminary data on the efficacy of the combination hydroxyurea (HU)/MBD: methotrexate (MTX)/bleomycin (BLEO)/cis-diamminedichloroplatinum (DDP) in advanced head and neck cancer.

PROTOCOL ENTRY CRITERIA: Patients with proved histologic diagnosis of squamous cancer of the head and neck (lymphoepitheliomas may also be entered) that is beyond hope of cure by either radiation or surgery. The disease must be evaluable and measurable. Hydrated serum creatinine must be less than 1.5 mg/dl and vital capacity and FEV-1 no less than 60 percent of predicted. WBC must be equal to or greater than 4000, platelet count 100,000/microliter. The patient must have received no prior treatment with any of the agents included in the present study and must have no evidence of obstructive uropathy.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; cis-Diamminedichloroplatinum, DDP, NSC-119875; Hydroxyurea, HU, NSC-32065; Methotrexate, MTX, NSC-740.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

HU - 2 g/sqm po on days 1 and 15; MTX - 40 mg/sqm im on days 1 and 15; BLEO - 10 U im on days 1, 8, and 15 (total dose limited to 400 U); DDP - 50 mg/sqm iv on day 4. Cycle to be repeated q 21 days for a minimum of 6 weeks and until progressive disease or prohibitive toxicity develops.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 50 mg vials; BLEO - 15 unit ampules; DDP - 10 mg vials; HU - 500 mg capsules.

DATE SUMMARIZED: 04/80

12.0004 PHASE III STUDY OF CHEMOTHERAPY WITH ADRIAMYCIN WITH VS WITHOUT CIS-DIAMMINE-DICHLOROPLATINUM FOR THYROID CARCINOMA

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PROTOCOL NUMBER(S) EST-2375

OBJECTIVES:

I. Determine and compare the therapeutic usefulness and toxicity of adriamycin alone or when combined with cis-diammine-dichloroplatinum.

PROTOCOL ENTRY CRITERIA: Patients with measurable lesions of inoperable thyroid cancer histologically classified as differentiated, medullary or anaplastic carcinoma. Patients with differentiated carcinoma must be refractive to iodine therapy and must have progressive disease on continuous suppressive therapy with thyroid hormones which must be maintained while on this study. All patients must have adequate cardiac, hepatic, renal and bone marrow functions, and a performance status of 3 or less.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: 2-Drug Combination Chemotherapy. cis-Platinum, DDP, NSC-119875; ADR.

STRATIFICATION BY: Participating institutions; histology: differentiated (including papillary and follicular) carcinoma, medullary or anaplastic (including small and giant cell) carcinoma; performance status: 0 or 1 vs. 2 or 3; metastatic spread: lymph nodes, visceral or cutaneous, or bone.

SPECIAL STUDY PARAMETERS: Thyrocalcitonin and T4-iodine or other thyroxine determination for patients with medullary carcinoma; audiogram and creatinine clearance for patients on DDP; bone scans.

END POINTS: Response/remission rate, objective tumor response, survival time, survival rate, response duration, toxicity/morbidity of treatment.

CURRENT STATUS: 182 patients will be entered.

DOSAGE SCHEDULE:

Arm I: ADR - 60 mg/sqm iv q 3 weeks for 18 weeks (total cumulative dose - 500 mg/sqm).

Arm II: ADR - as in Arm I. DDP - 40 mg/sqm iv q 3 weeks for 18 weeks.

For patients in Arms I and II increase ADR to 75 mg/sqm for the second course and thereafter if tolerated. Decrease initial dose to 45 mg/sqm for patients with prior radioiodine therapy with more than 500 millicuries or with prior radiotherapy of more than 3000 rad to more than 50% of the bone marrow. Escalate dosage of these patients to 60 mg/sqm in the second course and to 75 mg/sqm in the third course if tolerated. Discontinue therapy if disease progresses after 2 courses, if no response occurs after 3 courses, if EKG abnormality develops, and when maximum dose of ADR has been reached. Observe responders after total ADR dose has been given until relapse occurs.

Dosage modifications for toxicity and prior isotope or radiotherapy are given.

DOSAGE FORMS: ADR - 10 mg vials; DDP - 10 mg vials.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00380878

12.0005 PHASE II STUDY OF NEW AGENTS IN TREATMENT OF ADVANCED CANCER OF HEAD AND NECK: MGBG VS PALA

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PROTOCOL NUMBER(S) EST-2379

OBJECTIVES:

I. Determine effects of single-agent chemotherapy with methyl-GAG (MGBG) vs. PALA on advanced squamous cell cancer of head and neck.

PROTOCOL ENTRY CRITERIA: Patients with histologically-confirmed, measurable squamous cell cancer of the head and neck (including lymphoepitheliomas) with: metastases below the clavicles; no metastases below the clavicles but recurrent disease (following radiotherapy with or without surgery) that is uncontrollable locally by radiotherapy and/or surgery; or no metastases below the clavicles but with measurable residual tumor in treated area after at least 500 rads of irradiation if residual disease is biopsy proven more than 2 months after completion of radiotherapy and is not amenable to surgery. Patients must have adequate liver, kidney, and hematologic function, and an ECOG performance rating of at least 3. Patients must not: be eligible for ECOG protocols of higher priority; have surgery, radiotherapy or chemotherapy in prior 3 weeks (6 weeks for nitrosoureas or mitomycin); or have a greater than 15 percent weight loss in preceding 2 months if performance status is 2 or less (or greater than 10 percent if performance status is 3).

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Methyl-GAG, MGBG, NSC-32946.

Arm II: Single-agent Chemotherapy. PALA, NSC-224131.

STRATIFICATION: Participating institutions; ECOG performance status: 0 or 1 vs. 2 or 3; Stage: IV - distant metastases below clavicles vs. IV - no metastases below clavicles, but residual or recurrent disease above clavicles with N2 or N3 vs. IR, IIR, IIIR - no metastases below clavicles but residual or recurrent disease above clavicles T0, T1, T3 with N0 or N1.

SPECIAL STUDY PARAMETERS: CBC, liver and kidney function, tumor measurement, blood glucose.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 30 patients will be accrued for each drug.

DOSAGE SCHEDULE:

Arm I: MGBG - 600 mg/sqm iv over 30 minutes in 100 cc D5W q week for 2 weeks, then escalate to 700 mg/sqm q week.

Arm II: PALA - 3.75 g/sqm iv over 30 minutes in 250 cc D5W q 7 days.

Continue therapy for a minimum of 28 days. Thereafter remove from study patients with disease progression, toxicity requiring cessation of therapy for more than 6 weeks, or relapse after complete or partial response.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MGBG - 1 gm vials; PALA - 750 mg ampules.

DATE SUMMARIZED: 02/80

12.0006 PHASE III RADIOTHERAPY ALONE VS COMBINED WITH BLEOMYCIN CHEMOTHERAPY FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) NCOG-7H61

OBJECTIVES:

I. Determine the effect of radiation therapy with and without chemotherapy with bleomycin (BLEO) and methotrexate (MTX) used during induction, consolidation, and maintenance, on complete response and 3-year control of the primary tumor site and of regional lymph nodes, and duration of disease-free survival in patients with advanced inoperable squamous cell carcinoma of the head and neck.

II. Determine the effect of this therapy also on the prevention of metastatic disease in distant sites, overall survival time, and on normal tissues in patients treated with the combination radiotherapy and chemotherapy program.

PROTOCOL ENTRY CRITERIA: Surgically inoperable patients 35 to 70 years of age with measurable disease of biopsy-proven squamous-cell carcinoma of the oral cavity, pharynx or larynx, Stages III or IV (American Joint Committee Clinical Staging System 1977), without distant metastases. Patients must have adequate hematological functions, BUN not above 30, Karnofsky performance status less than 60% and an expected survival time of at least 10 weeks. The patients should not have had prior radiation or chemotherapy for their disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy alone.

Arm II: Induction: Radiotherapy plus Single-agent Chemotherapy. Cobalt-60 or 4 to 6 MeV X-rays; Bleomycin, BLEO, NSC-125066.

Maintenance: 2-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; BLEO.

STRATIFICATION BY: Participating institutions, tumor site, disease stage, reason for inoperability.

SPECIAL STUDY PARAMETERS: Kidney and liver function tests, scans and X-rays as indicated by tumor site and extent, bone scan, photograph of primary lesion.

END POINTS: Objective tumor response, response duration, survival time, toxicity/morbidity of treatment, quality of response, response/remission rate.

CURRENT STATUS: 240 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

Arm I: Radiotherapy to primary tumor, adjacent tissues and regional lymph nodes - 7000 rads minimal tumor dose given in no more than 50 fractions, 180 rads each, over a period of 10 weeks.

Arm II: Indu adiotherapy, as in Arm I, plus BLEO - 5.0 mg iv push twice a week at least 24 but no more than 72 hours apart during radiotherapy. If toxicity unacceptable, delay both Radiotherapy and BLEO.

Maintenance: Enter all patients from Induction. Begin 2 to 4 weeks after completion of Radiotherapy. BLEO - 15 mg iv push on day 1 q 7 days; MTX - 25 mg/sqm iv push on day 1 q 7 days. Give a total of 16 courses. Follow up all patients q month for the first year following therapy, q 2 months in the second year, and q 3 months thereafter until relapse, and until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 mg ampules; MTX - 5 and 50 mg vials.

DATE SUMMARIZED: 07/78

12.0007 PHASE III CHEMOTHERAPY WITH CACP VS CACP/MTX/CF FOR METASTATIC OR RECURRENT SQUAMOUS CELL CARCINOMA OF THE HEAD & NECK

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PROTOCOL NUMBER(S) NCOG-7H81

OBJECTIVES:

I. Compare effect of single-agent chemotherapy with cis-platinum (CACP) to combination chemotherapy with CACP/methotrexate (MTX) for metastatic or recurrent squamous cell carcinoma of the head and neck.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, metastatic or locally recurrent squamous cell carcinoma with primary site in oral cavity (oral tongue, buccal mucosa, floor of mouth), pharynx (base of tongue, tonsillar pillars or fossa, soft palate, oropharyngeal walls, pyriform sinuses, pharyngeal walls, post-cricoid region), larynx (epiglottis, aryepiglottic folds, arytenoids, false cords, laryngeal ventricle), and all sites within nasopharynx and sinuses. Patients must have a Karnofsky performance status of at least 60%, and adequate hematologic, kidney, and cardiac function. Patients must not have had prior chemotherapy with protocol drugs and must not have brain metastases.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: 3-Drug Combination Chemotherapy. CACP; Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590.

STRATIFICATION: Participating institutions; site of recurrent disease: locally recurrent vs. metastatic; primary site of disease: oral cavity vs. oropharynx vs. hypopharynx vs. larynx vs. nasopharynx vs. sinuses; performance status: 60%-70% vs. 80%-100%; radiation therapy: prior vs. no prior; chemotherapy: prior vs. no prior.

SPECIAL STUDY PARAMETERS: Performance status, angiogram, tumor dimension, adenopathy, bone and liver scan, liver size, E.M.I., skull films, urinalysis, magnesium, serum methotrexate level.

END POINTS: Response/remission rate, duration of response, recurrence rate, objective tumor response, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: 150 to 185 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: CACP - 80 mg/sqm given in 6 divided doses iv over 4 hrs each on day 1 q 3 weeks. Prehydrate patients over 4 hours and posthydrate for 24 hours so that urine output is at least 100 ml/hr over any 4 hour period.

Arm II: CACP - 80 mg/sqm infused as in Arm I; MTX - 250 mg/sqm iv infusion over 1 hour on days 1, 8, and 15 q 3 weeks. Prehydrate and posthydrate over 4 hours so that urine is over PH7; CF - 25 mg po at 24 hours, followed by 10 mg po q 6 hours for 6 doses on days 2, 9, and 16.

Continue therapy for 6 months. Give patients in complete remission 3 more months of treatment for Consolidation and then treat q 2 months until 2 years have elapsed. Remove from study patients in partial remission who progress.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; MTX - 2 mg and 50 mg vials.

DATE SUMMARIZED: 11/79

12.0008 NEUTRON RADIOTHERAPY FOR POTENTIALLY OPERABLE PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY, PHARYNX AND LARYNX

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PROTOCOL NUMBER(S) RTOG-7609

OBJECTIVES:

I. Assess the efficacy of neutron radiotherapy in terms of:

A. Absence of persistent or recurrent disease.

B. Length of survival, and tumor measurements and functional status at time of death.

C. Complications due to diverse forms of therapy.

D. Rehabilitation and functional status post therapy.

PROTOCOL ENTRY CRITERIA: Previously untreated and operable patients with squamous cell carcinoma of the oral cavity, oropharynx, supraglottic larynx or hypopharynx. Patients must not have distant metastases, two simultaneous tumors in the region under study, or prior chemotherapy or radical surgery or radiotherapy of the head and neck except for skin cancer.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Neutron irradiation only. (Arm no longer in November 1979 protocol edition.)

Arm II: Mixed Radiotherapy. Photon plus neutron irradiation.

Arm III: Radiotherapy plus Surgery. Neutron irradiation. (Photon irradiation added in November 1979 edition.)

Arm IV: Radiotherapy plus Surgery. Photon irradiation.

STRATIFICATION BY: Participating institutions; tumor site; extent of primary tumor: T2, T3, or T4.

SPECIAL STUDY PARAMETERS: Liver scan, endoscopy, chest x-ray, bone scan.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response, palpable nodes, presence or absence of metastases, rehabilitation.

CURRENT STATUS: About 280 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Neutron irradiation - 6600 to 7400 rad equivalent in 6 1/2 to 8 weeks, 4 fractions/week, using cyclotrons with neutron beams of 21.5 MeV or greater deuteron energy or 14 MeV D-T neutron generators. (Arm no longer in November 1979 protocol edition.)

Arm II: 6600 to 7400 rad eq/6 1/2 to 8 weeks/33 to 40 fractions, using 'mixed beams' consisting of 3 fractions of photons plus 2 fractions of neutrons/week. (Modified to 3 photons and 2 neutrons fractions/week, 4500 photons plus neutrons, ranging from 900 rad Fermi to 730 rad Seattle, in 7-8 weeks. Photons - 180-200 rad/fraction, 5 fractions/week. November 1979.)

Arm III: Radiotherapy: neutron irradiation - 5000 rad eq/20 to 22 fractions/5 to 5 1/2 weeks. (Modified to photon plus neutron as in Arm II. November 1979.) Surgery - Radical excision of the primary lesion, with or without neck dissection, within 4 to 6 weeks following completion of radiotherapy. (Surgery prior to or following Radiation. November 1979.)

Arm IV: Radiotherapy: Photon irradiation - 5000 rads/25 to 28 fractions/5 to 5 1/2 weeks using cobalt or megavoltage quality radiation. Surgery - same as in Arm III.

Deliver 5000 rad with photons or 5000 rad equivalent with neutrons or with mixed beams to the uninvolved neck area. Follow patients every 3 months for 2 years and then every 6 months for 3 years (total 5 years).

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 00100478

12.0009 NEUTRON AND/OR PHOTON RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY, PHARYNX AND LARYNX

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PROTOCOL NUMBER(S) RTOG-7610

OBJECTIVES:

I. Assess the clinical absence of local disease, or biopsy-proven evidence of recurrence.

II. Determine the length of survival, and tumor and functional status at time of death.

III. Assess the complications due to diverse forms of therapy.

IV: Assess post-therapy rehabilitation and functional status.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with squamous cell carcinoma of the oral cavity, oropharynx, supraglottic larynx, and hypopharynx; the primary lesions must be T2, T3 or T4 with nodes of any N staging. Patients must not have distant metastases or two simultaneous tumors in the region under study.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Photons only.

Arm II: Mixed Radiotherapy. 3 photon and 2 neutron fractions.

Arm III: Radiotherapy. Neutrons only.

STRATIFICATION BY: Participating institutions, region of the primary tumor, extent of the primary tumor (T2, T3, or T4).

SPECIAL STUDY PARAMETERS: Liver scan, endoscopic procedures, bone scan.

END POINTS: Response/remission rate, objective tumor response, length of survival, recurrence rate, toxicity/morbidity of treatment, survival rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Photons - 6600 to 7400 rads in 33 to 40 fractions given over 6 1/2 to 8 weeks, using megavoltage equipment operating at 4.0 MeV or greater or cobalt-60 with a minimum SSD of 80 cm. (Modified to 4400-5000 rad equivalents, using neutrons x equivalency factor, whenever possible. Treat lower neck with photons only. Photons at 180-200 rad/fraction. July 1979.)

Arm II: 3 fractions of photons plus 2 fractions of neutrons each week for a total dose of 6600 to 7400 rads in 33 to 40 fractions given in 6 1/2 to 8 weeks. (Modified to total of 4500 rads photons plus neutrons, ranging from 900 rad Fermi to 730 rad Seattle in 7-8 weeks. July 1979.)

Arm III: Neutrons - 6600 to 7400 rads of conventional LET photons given in 26 to 32 fractions in 6 1/2 to 8 weeks using cyclotrons with neutron beams of 21.5 MeV or greater deuteron energy or 14 MeV D-T neutron generators. Modified to 2400 rad Fermi to 1950 rad Seattle, 3-4 fractions/week over 7-8 weeks. July 1979.)

Deliver 5000 rad with photons or 5000 rad equivalent with neutrons or with mixed beams to the uninvolved neck area. At that point reduce treatment fields and include only palpable disease. Follow patients for 5 years. (Modified as above, July 1979.)

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/76

PATIENT ACCRUAL: 00690478

12.0010 PHASE II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS RADIOTHERAPY FOR RECURRENT HEAD AND NECK SQUAMOUS CELL CARCINOMA

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PROTOCOL NUMBER(S) RTOG-7802

OBJECTIVES:

I. Determine whether oral misonidazole combined with radiotherapy can improve the local control rates of advanced head and neck cancers without unacceptable side effects or late complications.

II. Study the acute and chronic drug effects determined in Phase I studies utilizing an advanced head and neck cancer patient population, while observing the tumor response of radiotherapy and sensitizer in combination.

III. Observe for possible therapeutic gain compared to historical controls, thereby aiding in the transition between the RTOG Phase I study and future randomization prospective multi-institutional protocols.

PROTOCOL ENTRY CRITERIA: Patients over 21 years of age with biopsy-confirmed, recurrent squamous cell carcinoma of the oral cavity, oropharynx, or hypopharynx. Patients must have moderately advanced to massive tumors, or tumors with low local control rates. Patients must have a minimum life expectancy of 4 months, and a Karnofsky level of at least 40%. Any prior therapy must have been terminated 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Radiosensitizer plus Radiotherapy. Misonidazole, NSC-261037, plus supervoltage Cobalt-60 or Clinac 4-6 MeV equipment.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Blood levels of Misonidazole, SMA-12/60, skin test for recall antigens, laryngogram, liver scan, neck tomogram.

END POINTS: Response/remission rate, objective tumor response, survival rate, toxicity/morbidity rate.

CURRENT STATUS: About 30 patients will be entered.

DOSAGE SCHEDULE:

Misonidazole - 2.5 gm/sqm po 4-5 hours before Radiotherapy on day 1 q week for 6 weeks. Give 5th and 6th doses only if no significant neurotoxicity has developed from a total dose exceeding 18 gms from the first 4 doses.

Radiotherapy: 250 rad given 3 hours after Misonidazole dose plus 210 rad 4 hours later on day 1, then 180 rad on days 2, 3 and 4. Repeat course q week for a maximum total of 6 courses, then give boost up to 1500 rad by interstitial Iridium-125 implants, Radium needles, Radon or Gold seeds, to primary or lymph node deposits. Assess patients monthly for the first year after Radiotherapy and every 3 months for the second year.

Remove from study patients with recurrences or at 24 months after the last therapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Misonidazole - 100 and 500 mg capsules.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00150179

12.0011 RADIOTHERAPY PLUS NEUTRON VS CONVENTIONAL BOOST FOR SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY, PHARYNX AND LARYNX

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PROTOCOL NUMBER(S) RTOG-7808

OBJECTIVES:

I. Determine the effect of a neutron boost to the primary and palpable neck nodes following conventional radiotherapy on local tumor control compared to a boost using conventional radiotherapy in Stage T2, T3 or T4 squamous carcinoma of the oral cavity, oropharynx, hypopharynx, or supraglottic larynx.

II. Determine the side effects and complications of neutron boost compared to conventional radiotherapy.

III. Determine the incidence of distant metastases for each treatment.

IV. Determine the survival and quality of survival for each treatment.

PROTOCOL ENTRY CRITERIA: Patients with localized, Stage T2, T3 or T4 squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, and supraglottic larynx. Patients must have a Karnofsky performance status of 50 or better and no prior chemotherapy or radical surgery or radiotherapy to the head and neck.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus boost Photon Radiotherapy. Equipment at 4 MeV or greater or Co-60 to the tumor region.

Arm II: Radiotherapy plus neutron boost Photon Radiotherapy. Equipment as in Arm I plus neutron beam boost.

STRATIFICATION BY: Participating institutions; region of primary: oral cavity and oropharynx vs. hypopharynx and supraglottic larynx; extent of primary: Stage T2 vs. T3 vs. T4.

SPECIAL STUDY PARAMETERS: Bone scan, hepatic function.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, incidence of metastases.

CURRENT STATUS: 140-160 patients to be entered in 2 to 2.5 years.

DOSAGE SCHEDULE:

Arm I: Radiotherapy plus boost 4500 to 5000 rad in 4.5 to 5.5 weeks to the primary tumor and affected lymph nodes plus the supraclavicular nodes. Photon boost 2500 to 3000 rad in 2.5 to 4 weeks to the primary only.

Arm II: Radiotherapy plus neutron boost Radiotherapy as above. Neutron boost 830 to 1000 rad in 2 to 3 weeks to the primary only.

Follow all patients q 3 months for 2 years then q 6 months for 3 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 02/80

12.0012 RADIOTHERAPY VS PION RADIOTHERAPY FOR STAGE III OR IV SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY AND PHARYNX

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PROTOCOL NUMBER(S) RTOG-7828

OBJECTIVES:

I. Determine in patients with Stage III and IV squamous cell carcinoma of the oral cavity and pharynx whether local tumor control of the primary is improved using pion radiotherapy compared to conventional treatment, whether the incidence of distant metastases is related to the various forms of treatment, and whether patient survival is improved with pion radiotherapy compared to conventional treatment.

II. Determine the morbidity of radiotherapy.

III. Assess the complications of therapy.

IV. Assess the quality of survival related to the various forms of treatment.

PROTOCOL ENTRY CRITERIA: Previously untreated patients between 18 and 75 years old with biopsy proven Stage III or IV squamous cell carcinoma of the oral cavity or oropharynx, nasopharynx or hypopharynx. Patients must have a Karnofsky performance status of 60 or better, no evidence of distant metastases and no prior definitive therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Conventional Radiotherapy or Radiotherapy plus Surgery. Cobalt teletherapy or supervoltage energy equipment. Radiotherapy alone. Patients with resectable tumors receive Radiotherapy plus Surgery.

Arm II: Pion Therapy at Los Alamos.

STRATIFICATION: Participating institutions; tumor region: oral cavity vs. oropharynx vs. nasopharynx vs. hypopharynx; Stage III vs. Stage IV; concomitant additional radiotherapy.

SPECIAL STUDY PARAMETERS: Liver, bone and brain scans; drawings and photographs, if possible, of primary and regional adenopathy.

END POINTS: Survival time, toxicity/morbidity of treatment, quality of survival, incidence of local recurrence and distant metastases, response/remission rate.

CURRENT STATUS: 150 to 180 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Minimum dose to the tumor - 6600 rad given in 6.5 to 7.5 weeks; maximum tumor dose to the boosted volume - 7500 rad in 7.5 to 9 weeks. Eligible patients receive presurgical Radiotherapy - 5000 rad in 5 to 6 weeks. Perform Surgery 3 to 5 weeks following completion of Radiotherapy - radical excision of the primary lesions with or without neck dissection.

Arm II: Pion Therapy - maximum of 3000 peak pion rad at a minimum of 85 peak pion rad/day. The minimum dose is approximately 2 cm peripheral to the 95% isodose line.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/79

HEAD AND NECK TUMORS

12.0013 PHASE I/II MISONIDAZOLE RADIOSENSITIZATION & HIGH FRACTIONAL DOSE RADIOTHERAPY FOR ADVANCED SQUAMOUS CELL HEAD AND NECK CANCER

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PROTOCOL NUMBER(S) RTOG-7904

OBJECTIVES:

I. Determine the effect of high fractional dose radiotherapy with vs. without misonidazole on nonresectable Stage III or IV or recurrent squamous cell carcinoma of the head and neck.

PROTOCOL ENTRY CRITERIA: Patients 18 to 75 years old with histologically confirmed, nonresectable or recurrent squamous cell carcinoma of the oral cavity, oropharynx, or hypopharynx of specified AJC Stages. Patients must have adequate hematologic, kidney, and liver function, acceptable neurologic and metabolic function, a life expectancy of at least 4 months, a Karnofsky performance status of at least 50%, and must not have had prior radiotherapy to the proposed target site.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Co-60, 4MeV or greater to primary tumor and palpable lymph nodes.

Arm II: Radiotherapy plus Single-agent Radiosensitization. Radiotherapy as in Arm I; plus Misonidazole, MNI, NSC-261037.

STRATIFICATION: Participating institutions; region of primary tumor: oral cavity vs. oropharynx or hypopharynx; stage: III vs. IV vs. recurrent; interstitial implant therapy: planned vs. not planned.

SPECIAL STUDY PARAMETERS: Neurological exam; radiographs; liver and kidney function; electrolytes; total protein and albumin; drug serum level.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival rate.

CURRENT STATUS: 70 patients will be entered in 1.5 years.

DOSAGE SCHEDULE:

Arm I: 4400 rad in 11 fractions with 5 fractions/week plus 400 rad on day following last fraction if clinically indicated.

Arm II: Radiotherapy, as in Arm I; MNI - 1.5 g/sqm (maximum total dose 10.5 mg/sqm) po in 3 doses/week for a total of 7 doses given 4 to 6 hours prior to Radiotherapy. Follow patients until death.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 10/79

12.0014 LIMITED VS RADICAL NECK DISSECTION PLUS PRE- OR POSTOPERATIVE RADIOTHERAPY FOR HEAD AND NECK CARCINOMA WITH CLINICALLY POSITIVE NODES

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PROTOCOL NUMBER(S) RTOG-7912

OBJECTIVES:

I. Determine the efficacy in terms of local control of limited vs. radical neck dissection combined with preoperative or postoperative radiation therapy in patients with squamous cell carcinoma of the head and neck with metastases to the cervical lymph nodes.

II. Determine the morbidity and complication rate of limited vs. radical neck dissections, each combined with radiation therapy.

III. Determine the incidence of distant metastases and survival in each treatment group.

PROTOCOL ENTRY CRITERIA: Patients with previously untreated, biopsy proven head and neck primary squamous cell carcinoma or lymphoendothelioma presenting with palpable cervical nodes, primary sites unknown. Primary sites may include the oral cavity, the oropharynx, the hypopharynx, or the larynx, but not the nasopharynx. Patients may not have massive cervical nodes or clinically positive nodes in the posterior cervical triangle, nor may there be distant metastases or a history of a previous malignancy in the head and neck regions except primary skin cancer. The Karnofsky score must be greater than 60.

PROTOCOL OUTLINE: Randomized study. Patients are assigned to Regimen A or Regimen B prior to randomization to Arm I or II.

Regimen A: Preoperative Radiotherapy. Megavoltage equipment (Co-60 equal to or greater than 2 MeV, electron energies of 5-25 MeV alone or combined with photons).

Regimen B: Postoperative Radiotherapy. Equipment as in Arm I.

Arm I: Surgery. Radical neck dissection.

Arm II: Surgery. Limited neck dissection.

STRATIFICATION BY: Participating institutions, time of radiotherapy (before vs. after surgery), N status (N-1 vs. N-2A vs. N-2B vs. N-3B vs. N-3C), site of primary (oral cavity vs. oropharynx vs. larynx vs. hypopharynx).

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Local control of cervical node metastases, appearance of newly involved nodes within irradiated clinically negative areas, incidence of distant metastases, complication rate, morbidity associated with treatment, duration of survival, causes of failure, functional status of patients.

CURRENT STATUS: 150 patients will be required in each surgical arm and are anticipated to have been accrued within 4 years; an additional 2 years will be required for follow-up.

DOSAGE SCHEDULE:

Regimen A: Tumor volume dose of 4600-5000 rads in 4.5-5.5 weeks. Surgery to be performed 5-6 weeks after completion of radiation therapy.

Regimen B: Beginning during the third or fourth week following surgery, tumor volume dose of 5000 rads in 5-5.5 weeks. Increase to 6000 rads in 6-7 weeks for any area suspected to have residual disease or where neoplastic cells are seen within 5 mm of the surgical border; increase to 7000 rads for areas of gross residual disease at the time of commencement of Radiotherapy.

Arm I: Radical neck dissection, resecting the primary lesion at the same time and in continuity with the neck dissection whenever possible.

Arm II: Limited neck dissection, resecting the primary lesion at the same time and in continuity with the neck dissection whenever possible.

Dosage modifications for toxicity are not applicable.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 08/80

12.0015 HYPERFRACTIONATED VS CONVENTIONAL RADIOTHERAPY FOR ADVANCED CARCINOMA OF THE ORAL CAVITY, PHARYNX, LARYNX OR SINUSES

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PROTOCOL NUMBER(S) RTOG-7913

OBJECTIVES:

I. Determine whether local control of primary head and neck carcinoma can be improved (over conventional fractionation) with hyperfractionation.

II. Evaluate patient acceptance and tolerance of normal tissue to twice daily fractionated treatment.

III. Determine whether inoperable lesions can be made operable by an altered fractionated technique of administering radiation therapy.

IV. Determine survival rates of each fractionation technique.

PROTOCOL ENTRY CRITERIA: Patients over 18 years old without previous treatment of Stage III or IV carcinoma of the oral cavity, oropharynx, hypopharynx, or any stage disease of the nasopharynx or maxillary sinus. Patients must have a biopsy proven carcinoma but not adenocarcinoma and no evidence of metastases, plus a Karnofsky performance status of 60 or higher. Patients must have adequate hepatic and nutritional status, and must not be eligible for entry to SWOG-7915, or for surgery following radiotherapy.

PROTOCOL OUTLINE: Randomized study. Use Cobalt-60, 4 MeV or higher equipment.

Arm I: Conventional Radiotherapy.

Arm II: Hyperfractionated Radiotherapy.

STRATIFICATION: Participating institutions; AJC tumor Stage III vs. IV; site of primary: oral cavity, oropharynx vs. hypopharynx; maxillary sinus vs. nasopharynx, vs. supraglottic larynx.

SPECIAL STUDY PARAMETERS: Hepatic function serology.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, objective tumor response.

CURRENT STATUS: 400 patients will be entered in 2 to 4 years.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 6600 to 7000 rad given in 5 weeks, as 180 to 200 rad per day, 5 days per week.

Arm II: Radiotherapy - 6000 rad given in 5 weeks, as two daily doses of 120 rad separated by 3 to 6 hours, 5 days per week.

Irradiate primary tumor and regional nodes at each treatment session according to site-specific techniques as specified in the protocol.

Follow up all patients q 3 months in the first 2 years, q 6 months for 3 years and then annually.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/79

12.0016 PHASE III ADJUVANT CHEMOTHERAPY WITH CIS-PLATINUM FOR DEFINITIVELY TREATED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) RTOG-7914

OBJECTIVES:

I. Determine whether cis-platinum (CACP) adjuvant chemotherapy will effectively (a) decrease the incidence of distant metastases, (b) decrease the incidence of local-regional recurrence, (c) increase the total length of the disease-free interval, and (d) improve survival in patients with Stages III and IV squamous cell carcinoma of the head and neck who have achieved total tumor clearance with initial surgery and/or radiation therapy.

II. Determine the toxicity of maintenance cis-platinum adjuvant chemotherapy with particular attention to the nutritional and performance status of the patient.

PROTOCOL ENTRY CRITERIA: Patients between 30 and 70 years of age with biopsy-proven Stage III or IV squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx. They must be clinically free of disease following curative radiotherapy or surgery plus radiotherapy and must be within 90-120 days (90-150 days, per August 1980 revision) of the initiation of that definitive treatment. Patients must have a performance status above 50 and adequate renal, hepatic, hematologic, cardiac and pulmonary status. The primary lesion must have been T2 with positive nodes or T3, T4 with any nodal status.

PROTOCOL OUTLINE: Randomized study.

Arm I: No therapy.

Arm II: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION: Participating institutions: disease site: larynx-glottis; vs. larynx-supraglottis vs. oral cavity vs. oropharynx vs. hypopharynx; disease stage: III vs. IV; initial therapy: radiotherapy vs. radiotherapy plus surgery.

SPECIAL STUDY PARAMETERS: Liver and bone scans, electrolytes, nutritional assessment, audiogram.

END POINTS: Recurrence rate, disease-free interval, survival time.

CURRENT STATUS: 70 patients per year will be entered for 3 years.

DOSAGE SCHEDULE:

Arm I: No therapy.

Arm II: CACP - 50 mg/sqm iv on days 1 and 8 with adequate hydration. Enter patients within 90 to 120 days (90-150 days, per August 1980 revision) of initiation and within 28 to 56 days of completion of initial definitive treatment with radiotherapy with or without surgery.

Repeat course q 28 days provided toxicity has abated, for 6 cycles. Follow all patients for recurrence and survival at least 3 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 12/79

12.0017 PHASE III RADIOTHERAPY WITH OR WITHOUT MISONIDAZOLE FOR LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) RTOG-7915

OBJECTIVES:

I. Determine whether once weekly oral misonidazole (MNI) combined with radiotherapy can improve the local control rate (primary and regional nodes) of advanced head and neck cancers without unacceptable side effects or late complications, compared to conventional radiotherapy alone.

II. Determine whether MNI will enhance the 2-year and 5-year tumor-free survival (cure) attained in this patient population.

III. Study late effects of the combined treatment upon normal tissues (skin/mucosa) included in the irradiated regions.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven, inoperable squamous cell carcinoma of the head and neck. Patients must have a Karnofsky performance status of 60 or better and be between 18 and 70 years old. Patients must have no prior therapy to the area under study and must have adequate renal, hematologic and neurologic status.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Co-60 energy or greater to the primary and surrounding regions.

Arm II: Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037; Radiotherapy as in Arm I.

STRATIFICATION BY: Participating institutions; region of primary: oral cavity, supraglottic larynx, oropharynx (except base of tongue) vs. oropharynx (base of tongue), nasopharynx, maxillary sinus; disease stage: Stage II vs. III vs. IV.

SPECIAL STUDY PARAMETERS: SMA-12/60, liver and bone scans, laryngogram.

END POINTS: Response/remission rate, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: At least 300 patients to be entered.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 6600 to 7380 rad in 6.5 to 8 weeks to the primary and surrounding structures.

Arm II: MNI - 2 g/sqm (12 g/sqm maximum cumulative dose) po on day 1, 4 to 6 hours prior to Radiotherapy. Repeat q 7 days for 3 courses. Radiotherapy as in Arm I.

Follow all patients q 3 months for 1.5 years, then q 4 months for 3 years.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 02/80

12.0018 PILOT STUDY OF DIBROMODULCITOL FOR SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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Birmingham, Tumor Inst., Room 225, Birmingham, Alabama,
35294, United States of America
PROTOCOL NUMBER(S) SEG-HN-P44

OBJECTIVES:

I. Determine the effectiveness of dibromodulcitol in squamous cell carcinoma of the head and neck.

PROTOCOL ENTRY CRITERIA: Patients 18 years of age and older with histologically diagnosed and measurable squamous cell carcinoma of the head and neck. Patients must have recurrent disease or be incurable following surgery or radiotherapy and must have failed or be ineligible for higher priority SEG studies. Patients must have had no chemotherapy or radiotherapy four weeks prior to present treatment nor another active malignancy. Patients must have a Karnofsky status of 50 or more, a life expectancy of at least 6 weeks and adequate hematologic, liver and kidney functions.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dibromodulcitol, DBD, NSC-104800.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Bone and liver scan, liver function tests, tumor measurements.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response.

CURRENT STATUS: 25 to 29 patients will be entered.

DOSAGE SCHEDULE:

DBD - 180 mg/sqm po every day at bedtime (qhs) on days 1 through 10 q 28 days. Increase DBD to 190 mg/sqm qhs for the second course if granulocyte and platelet counts remain adequate.

Evaluate patients prior to each course of therapy after the second course. If grade 2 toxicity or prolonged hematologic depression occurs reduce DBD to 180 mg/sqm. Lower dose of DBD to 150 mg/sqm for grade 3 toxicity. Remove patients with disease progression from study. Continue therapy for responders and those with stable disease until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DBD - 25 and 50 mg tablets.

DATE SUMMARIZED: 11/79

12.0019 PHASE II CHEMOTHERAPY WITH ADR/CACP FOR ADVANCED THYROID CANCER

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Comprehensive Cancer Center, University of Alabama,
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35294, United States of America
PROTOCOL NUMBER(S) SEG-78THY0102; SEG-78THY225

OBJECTIVES:

I. Determine the objective response rate and duration of response of therapy with adriamycin (ADR) and cis-platinum (CACP) in patients with disseminated thyroid cancer.

II. Assess the quantitative and qualitative toxicity of this combination.

PROTOCOL ENTRY CRITERIA: Patients with measurable thyroid carcinoma, unresectable or metastatic and unsuitable for radio-iodine (I-131) therapy. Patients must have adequate blood counts and renal function and must not have had prior chemotherapy with ADR or CACP.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: EKG, audiometry, tests of renal and hepatic function, bone and liver scans, calcitonin.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: About 30 patients will be entered.

DOSAGE SCHEDULE:

ADR - 60 mg/sqm iv (maximum cumulative dose 450 mg/sqm) increased to 75 mg/sqm in subsequent doses if there is no Grade 1 hematologic toxicity after the 1st course. CACP - 60 mg/sqm iv increased to 75 mg/sqm if subsequent serum creatinine is less than 1.5 mg%. Repeat course q 28 days. Evaluate patients after 2 courses and remove nonresponders from study. Continue therapy until maximum ADR is reached or progression occurs.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; ADR - 10 and 50 mg vials.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00031078

12.0020 PHASE II PVB (CACP/VBL/BLEO) VS MTX FOR RECURRENT OR METASTATIC SQUAMOUS CELL CARCINOMA OF HEAD AND NECK ORIGIN

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Birmingham, Tumor Inst., Room 225, Birmingham, Alabama,
35294, United States of America
PROTOCOL NUMBER(S) SEG-79HN235

OBJECTIVES:

I. Determine the efficacy and toxicity of combination chemotherapy with PVB: cis-platinum (CACP)/vinblastine (VBL)/bleomycin (BLEO) vs. methotrexate (MTX) for recurrent or metastatic squamous cell cancer of head or neck origin.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, recurrent or metastatic squamous cell carcinoma of the oral cavity, oropharynx, nasopharynx, paranasal sinuses, supraglottic or glottic larynx not amenable to other modalities of treatment. Patients must have a Karnofsky performance status of at least 50% and adequate kidney and liver function and must not have received prior chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Induction:

Arm I: 3-Drug Combination Chemotherapy. PVB: Cis-platinum, CACP, NSC-119785; Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066.

Arm II: Single-agent Chemotherapy. Methotrexate, MTX, NSC-740.

STRATIFICATION: Participating institutions; prior radiotherapy and/or surgery; location of metastasis: below clavicle vs. locoregional.

SPECIAL STUDY PARAMETERS: Audiometry; bone and liver scan.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, length of survival.

CURRENT STATUS: 58 patients will be entered in 2.5 years.

DOSAGE SCHEDULE:

Arm I: PVB: CACP - 60 mg/sqm iv slow infusion (1 mg/min) with adequate hydration; VBL - 0.1 mg/kg iv push on days 1 and 15; BLEO - 15 U iv push on days 1, 8, 15 and 22.

Repeat at 29 days for a total of 2 courses.

Arm II: MTX - 45 mg/sqm iv push q 7 days. Evaluate patients after 8 weeks. Continue PVB for 5 courses or MTX for 20 courses for patients with complete or partial response or without disease progression. Remove from study patients who progress at any time.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 and 25 mg vials; BLEO - 15 mg ampules; VBL - 10 mg ampules; MTX - 5 and 50 mg vials.

DATE SUMMARIZED: 10/79

HEAD AND NECK TUMORS

12.0021 SURGERY & RADIOTHERAPY WITH OR WITHOUT MTX/CF/BLEO/CACP FOR STAGE III OR IV EPIDERMOID CANCER OF THE MOUTH, HYPOPHARYNX, LARYNX

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PROTOCOL NUMBER(S) SEG-79HN356

OBJECTIVES:

I. Determine the response rate of previously untreated patients with epidermoid carcinoma of the oral cavity (anterior tongue, floor of mouth, retromolar trigone, lower alveolar ridge) of the hypopharynx (pyriform sinus) and larynx (supraglottic and glottic) to a combination chemotherapy regimen of cis-platinum (CACP), bleomycin (BLEO) and methotrexate (MTX) with citrovorum factor (CF) rescue.

II. Compare the survival and disease-free interval of patients treated with pre-operative chemotherapy with those of patients treated with identical surgical and post-operative radiotherapeutic techniques without chemotherapy.

III. Compare the toxicities and complications of the two programs.

PROTOCOL ENTRY CRITERIA: Patients less than 75 years of age with Stage III or IV epidermoid carcinoma of the oral cavity, hypopharynx or larynx. Patients with T1,2; N1; N0 carcinoma of the supraglottic and glottic larynx and hypopharynx and those with T4 or N3 lesions are ineligible. Patients must have adequate serum protein, albumin and renal function values and they must not have lost more than 10% of their normal body weight in the two months prior to treatment.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy plus Surgery and Radiotherapy. Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875; followed by Surgery plus post-operative radiation therapy with Cobalt-60 or x-ray generators with a peak photon energy of 2 MeV or more.

Arm II: Surgery plus Radiotherapy.

STRATIFICATION: Participating institutions; disease stage; extent of tumor.

SPECIAL STUDY PARAMETERS: SMA-12; liver and bone scan; lung tomography; creatinine clearance.

END POINTS: Response/remission rate; duration of response; toxicity/morbidity of treatment; survival rate; length of survival; disease-free survival time.

CURRENT STATUS: 660 patients will be entered in 3 to 4 years.

DOSAGE SCHEDULE:

Arm I: MTX - 280 mg/sqm/day iv push in 4 divided doses on day 0 and 21; CF - 6 mg iv push q 6 hrs starting 36 hrs after 1st dose of MTX for 9 doses; BLEO - 30 mg iv push q week for 6 weeks starting on day 0; CACP - 2 mg/kg iv drip given in 1 hour in 200 ml saline on days 3 and 24 with mannitol diuresis. Evaluate patients after one course. Hold second course of MTX and CACP if bone marrow is depressed and continue BLEO - 30 mg iv push q 7 days for 4 weeks. Proceed to surgery within 28 days of the second CACP dose or, if 2nd course is postponed due to bone marrow depression, no later than day 52 after beginning of therapy. Following surgery evaluate patients. Remove patients with metastatic disease or unresectable disease from study. Give radiotherapy to patients with no metastatic disease within 56 days or surgery. Radiotherapy - 5500-6000 rad given within 5 to 7 weeks to original primary and node-bearing region.

Arm II: Surgery followed in 60 days by Radiotherapy as in Arm I.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; MTX - 5 and 50 mg vials; BLEO - 15 unit vials; CF - 3 mg ampules.

DATE SUMMARIZED: 11/79

12.0022 MTX/CF/BLEO/CACP AND RADIOTHERAPY WITH OR WITHOUT SURGERY FOR STAGE IV EPIDERMOID CANCER OF THE MOUTH, LARYNX & HYPOPHARYNX

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PROTOCOL NUMBER(S) SEG-79HN357

OBJECTIVES:

I. Determine the response rate of previously untreated patients with inoperable Stage IV epidermoid carcinoma of the floor of the mouth, anterior tongue, anterior tonsillar pillar, and retromolar trigone areas to combination chemotherapy with cis-platinum (CACP), bleomycin (BLEO) and methotrexate (MTX) with citrovorum factor (CF) rescue.

II. Determine the percentage of responding patients rendered operable by a combination of CACP, BLEO and MTX with CF rescue, followed by radiation therapy.

III. Compare the disease-free survival and survival of the patients rendered operable with that of a historical control and with that of those not rendered operable.

PROTOCOL ENTRY CRITERIA: Patients less than 75 years of age with Stage IV epidermoid carcinoma of the oral cavity (anterior tongue, floor of mouth, retromolar trigone and lower alveolar ridge), larynx and hypopharynx (pyriform sinus). Patients must have no other uncontrolled primary cancer nor have lost more than 10% of their normal body weight. Patients must have adequate serum albumin, serum protein and renal function.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy plus Radiotherapy plus Surgery. Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590; Bleomycin, BLEO, NSC-125066; plus Radiotherapy with Cobalt-60 or x-ray generators of 2 MeV or more. Clinically operable patients undergo definitive Surgery.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: SMA-12; liver and bone scan; lung tomography; creatinine clearance.

END POINTS: Response/remission rate; survival rate; objective tumor response; toxicity/morbidity of treatment.

CURRENT STATUS: About 70 patients will be entered.

DOSAGE SCHEDULE:

Induction:

MTX - 280 mg/sqm/day iv push in 4 divided doses on days 0 and 21. If no toxicity occurs increase dose to 560 mg/sqm/day for the second course; CF - 54 mg in 9 divided doses beginning 36 hours after first dose of MTX; BLEO - 30 mg iv push q 7 days for 6 weeks starting on day 0; CACP - 2 mg/kg iv drip given in 1 hour on days 3 and 24 with mannitol diuresis. Continue Chemotherapy for 2 courses. Begin Radiotherapy between day 45 and 59, 4,000-5,000 rads given over 4 to 5 weeks to the original primary and node bearing region. Perform excision of primary tumor and radical neck dissection for involved cervical lymph nodes within 56 days of completion of Radiotherapy. Evaluate patients for involved margins and metastatic disease. Follow for disease-free survival and total survival. Follow clinically inoperable patients for survival.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; MTX - 5 and 50 mg vials; BLEO - 15 unit bottles; CF - 3 mg ampules.

DATE SUMMARIZED: 11/79

12.0023 PHASE III CHEMOTHERAPY WITH COB (CACP/VCR/BLEO) PLUS RADIOTHERAPY AND SURGERY VS RADIOTHERAPY PLUS SURGERY FOR HEAD AND NECK CANCER

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7902

OBJECTIVES:

I. Compare the survival of patients with Stage III and IV squamous cell carcinoma of the tongue, oral cavity, tonsil, oropharynx, hypopharynx and larynx subjected to radiation therapy followed by surgical excision if possible, versus survival of patients subjected to chemotherapy with cis-platinum (CACP), vincristine (Oncovin, VCR), and bleomycin (BLEO), followed by radiation therapy and surgical excision if possible.

II. Determine the incidence and extent of complications arising from chemotherapy and radiotherapy followed by head and neck surgery versus radiotherapy and head and neck surgery.

PROTOCOL ENTRY CRITERIA: Previously untreated patients who have a histologically confirmed diagnosis of squamous cell carcinoma of the oral cavity, tongue, tonsil, oropharynx, hypopharynx or larynx, Stages III and IV, with no evidence of distant metastases. All patients must have a nonresectable, evaluable lesion, such as one that has radiographically eroded a portion of skull or cervical spine, or is fixed to the common, external, or internal carotid arteries. The ultimate decision of operability rests on the expertise of the oncologic surgeon. Patients must have a life expectancy of 6 weeks or greater, a good performance status (0-3), no significant obstructive uropathy from an enlarged prostate, and adequate bone marrow, pulmonary, and renal functions.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Radiotherapy plus Surgery. COB: cis-Platinum, CACP, NSC-119875; Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066. Cobalt-60 or megavoltage x-ray.

Arm II: Radiotherapy plus Surgery. Cobalt-60 or megavoltage x-ray.

STRATIFICATION BY: Disease stage, site of tumor, participating institutions, performance status.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 100 patients/year will be entered. Approximately 40 patients/arm are required for significant results from study.

DOSAGE SCHEDULE:

Arm I: COB: CACP - 100 mg/sqm iv on days 1 and 22; VCR - 1 mg iv on days 2 and 5; BLEO - 30 units iv on days 2 through 5. Repeat course one time. On days 43-67, Cobalt-60 or 2-6 MeV x-ray - 5000 rads in 200-rad fractions, 5 fractions/week. At 2 weeks post-Radiotherapy, patient is evaluated for possible surgery. If patient still inoperable, an additional 1600 rads will be delivered; if operable, radical surgery will be performed within 4 to 6 weeks post-Radiotherapy.

Arm II: Cobalt-60 or 2-6 MeV x-ray - as in Arm I.

All patients free of residual disease following treatment will undergo observation for local or systemic relapse; those patients with residual disease will go off study. All patients will be followed for life.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials; BLEO - 15 unit ampules; VCR - 1 and 5 mg vials.

DATE SUMMARIZED: 05/80

12.0024 PHASE II CHEMOTHERAPY WITH ADR/CTX/5-FU FOR ADVANCED CARCINOMA OF THE SALIVARY GLAND

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7915

OBJECTIVES:

I. Determine the effects of adriamycin (ADR)/cyclophosphamide (CTX)/5-fluorouracil (5-FU) for advanced, rapidly growing epithelial tumors of the salivary glands not amenable to surgery or radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, aggressively and actively growing epithelial tumor arising in one of the major (symetrically paired parotid, submaxillary or sublingual) or minor (mucus-secreting) salivary glands, not amenable to surgery or radiotherapy. Patients must have adequate bone marrow and liver function and normal kidney function, and must not have had prior chemotherapy or current or prior congestive heart failure.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION: Participating institutions; histology: high-grade mucoepidermoid vs. other.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 25 patients will be entered in 1.5 years.

DOSAGE SCHEDULE:

ADR - 40 mg/sqm (25 mg/sqm for patients with impaired liver function, maximum total dose 450 mg/sqm) iv on day 1; CTX - 400 mg/sqm iv on day 1; 5-FU - 400 mg/sqm iv on days 1 and 8, all q 21 days for 2 courses if there is adequate hematologic status. Keep patients on study until progression, unsatisfactory stable disease, or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules; CTX - 100 and 500 mg ampules; 5-FU - 500 mg ampules.

DATE SUMMARIZED: 11/79

12.0025 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE FOR METASTATIC OR LOCALLY RECURRENT SQUAMOUS CELL CARCINOMA OF THE HEAD & NECK

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PROTOCOL NUMBER(S) SWOG-7923

OBJECTIVES:

I. Determine the efficacy as determined by response rate of gallium nitrate in patients with metastatic and/or local recurrent squamous cell carcinoma of the head and neck who have failed on higher priority treatment protocols.

II. Determine whether gallium scan results may be predictive of antitumor effect.

PROTOCOL ENTRY CRITERIA: Patients with clearly observable or measurable, histologically proven, incurable, advanced metastatic or locally recurrent squamous cell carcinoma of the head and neck. Patients must have adequate cardiac, hematologic, kidney and liver function, a life expectancy of at least 6 weeks and a Karnofsky performance status of 50 to 60. Prior therapy must have terminated at least 4 weeks prior to entry with evidence of hematologic recovery.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Gallium nitrate, NSC-15200.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: 24-hour urine protein and creatinine clearance, gallium scan, audiogram.

END POINTS: Response/remission rate, objective tumor response, recurrence rate, response duration, survival time, toxicity/morbidity of treatment.

CURRENT STATUS: 14 to 25 patients will be entered.

DOSAGE SCHEDULE:

Patients must be adequately hydrated prior to therapy. Gallium nitrate - 700 mg/sqm iv 30-min infusion given q 14 days if toxicity permits. Give a minimum of 2 courses. Remove from study patients with increasing or unsatisfactory stable disease, or patients developing severe renal toxicity or clinical hearing loss.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Gallium nitrate - 100 mg ampules.

DATE SUMMARIZED: 12/79

HEAD AND NECK TUMORS

12.0026 PHASE II CHEMOTHERAPY WITH AMSA FOR METASTATIC SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) SWOG-7934

OBJECTIVES:

I. Determine the antitumor activity/response rate and duration of response in patients with metastatic squamous cell carcinoma of the head and neck who have failed on higher priority protocols.

II. Determine the nature and degree of toxicity of this drug.

PROTOCOL ENTRY CRITERIA: Patients with measurable histologically proven, incurable advanced squamous cell carcinoma of the head and neck. Patients must have a minimum life expectancy of 6 weeks, a SWOG performance status of 2 or better, and adequate hematologic and liver function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Participating institutions; prior chemotherapy: adriamycin vs. other vs. none; risk status: good vs. poor.

SPECIAL STUDY PARAMETERS: Hepatic function.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, duration of response, duration of survival, relapse rate.

CURRENT STATUS: At least 14 to 25 patients to be entered in 6 months.

DOSAGE SCHEDULE:

AMSA - 40 mg/sqm (start poor-risk patients, those over 65, with prior chemotherapy or impaired bone marrow, hepatic or renal status at 30 mg/sqm) iv on days 1 through 3. Repeat q 21 days or as toxicity permits. Remove patients from study after 2 courses when disease progresses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 20 mg and 75 mg ampules

DATE SUMMARIZED: 02/80

12.0027 PHASE III SURGERY & RADIOTHERAPY WITH/WITHOUT PREOPERATIVE BLEO/CACP/MTX/VCR FOR STAGE III/IV EPIDERMOID CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) SWOG-8006

OBJECTIVES:

I. Determine the length of remission, recurrence rates, survival rates and pattern of recurrence for patients receiving therapy utilizing surgery and postoperative radiation vs. combined therapy utilizing preoperative chemotherapy with bleomycin (BLEO), cis-platinum (CACP), methotrexate (MTX) and vincristine (VCR), surgery and postoperative radiation therapy for operable Stage III or IV epidermoid carcinoma of the head and neck.

PROTOCOL ENTRY CRITERIA: Patients with resectable Stage III or IV epidermoid carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx. Patients must have a histologically confirmed diagnosis of squamous cell carcinoma that is evaluable. A life expectancy of 6 months or longer and a performance status of 3 or better are required. There must be an initial WBC of 3000/cumm or greater and a platelet count of 100,000/cumm or greater, as well as a minimum creatinine clearance of 50 cc/minute. Patients must have adequate pulmonary function and must be evaluated for entry by head and neck surgeon, radiation oncologist and medical oncologist. Prechemotherapy biopsy material and postchemotherapy pathologic material must be submitted for each patient entering the study.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery plus Radiotherapy. Cobalt Teletherapy or Linear Accelerator, 4 MeV or greater.

Arm II: 4-Drug Combination Chemotherapy plus Surgery plus Radiotherapy. Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875; Methotrexate, MTX, NSC-740; Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Site of primary tumor: oral cavity, oropharynx, hypopharynx or larynx; performance status: 0-1 vs. 2 or greater; participating institutions.

SPECIAL STUDY PARAMETERS: PO2, DCLO vital capacity; audiometry; IVP; chest, skull, cervical spine x-rays; hematologic, renal and hepatic function tests.

END POINTS: Response/remission rate, survival rate, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 135 patients will be entered over 16 months.

DOSAGE SCHEDULE:

Arm I: Complete removal of primary tumor with large safety margin. If positive neck disease, radical neck dissection concomitant with tumor removal. Radiotherapy is initiated 4 to 8 weeks following Surgery, when sufficient healing has occurred, at a dose of 5000 rads in 5 weeks to site of resected primary. If there is evidence of residual disease, dose may be increased to 6500 rads in 6.5 weeks.

Arm II: BLEO - 15 U/sqm iv or im on days 1 and 8; CACP - 50 mg/sqm iv on day 1; MTX - 40 mg/sqm iv on day 1; VCR - 2 mg iv on day 1. Repeat q 21 days for 3 courses. Rest for 3 weeks, then Surgery and Radiotherapy as in Arm I.

All patients will be followed until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BLEO - 15 U ampules; CACP - 10 mg vials. Other drug forms are not given.

DATE SUMMARIZED: 10/80

12.0028 COMBINATION CHEMOTHERAPY WITH CTX/CACP FOR ADVANCED, RECURRENT EPIDERMOID CARCINOMA OF THE HEAD AND NECK

Forastiere, A. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-8026

OBJECTIVES:

I. Evaluate the response rate and duration of response of the combination of cyclophosphamide (CTX) and cis-platinum (CACP) in previously treated patients with epidermoid carcinoma of the head and neck.

II. Assess the toxicity associated with this two-drug regimen.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, epidermoid carcinoma with a primary site in the head and neck area who have failed primary treatment (surgery and/or radiotherapy). Patients must have a Karnofsky performance status greater than 50 percent; there must be adequate hematologic, renal, and hepatic function. No prior treatment with cis-platinum or cyclophosphamide is allowed (except if given prior to surgery and/or radiotherapy as adjuvant treatment). Patients must not receive radiotherapy within the 4 weeks prior to entry. There must be no history of malignancy except for basal cell carcinoma of the skin.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; EKG; SMA-6; SMA-12; CXR; bone and liver scans; CAT scan; base of skull tomograms; tumor measurements.

END POINTS: Response/remission rate, objective tumor response, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: The required protocol population is 25 patients.

DOSAGE SCHEDULE:

CACP - 60 mg/sqm iv infusion over 3 hours with pre- and posthydration; CTX - 600 mg/sqm bolus injection into a freely running iv infusion. Repeat treatment q 3 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

12.0029 PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE (AZQ) FOR ADVANCED EPIDERMOID CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) BCRP-8028

OBJECTIVES:

I. Determine the response rate and duration of response in previously treated patients with epidermoid carcinoma of the head and neck treated with aziridinylbenzoquinone, AZQ, administered as a single dose every three weeks.

II. Assess the toxicity associated with AZQ in the dose and schedule used in this Phase II study.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, measurable, epidermoid carcinoma with a primary site in the head and neck area who have failed primary treatment (surgery and/or radiotherapy). Patients must have a life expectancy of at least 8 weeks; the Karnofsky performance status must be at least 50 percent; and there must be adequate bone marrow reserve, renal function, and no evidence of obstructive liver disease. There must be no history of a malignancy except for curatively treated basal cell carcinoma of the skin or surgically treated carcinoma in situ of the cervix. Patients must not receive chemotherapy or radiotherapy within the 4 weeks prior to entry (8 weeks for nitrosoureas) unless there is evidence of rapid tumor progression.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Aziridinylbenzoquinone, AZQ, NSC-182986.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; tumor measurements; scintiscans, x-rays; EKG; tomograms of base of skull.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Initially, 14 patients will be entered. If there is a response to the drug, a total of 20-30 patients will be entered.

DOSAGE SCHEDULE:

AZQ - 20 mg/sqm through a freely running iv infusion over 15-30 minutes on days 1 and 8. Treatment is repeated q 28 days. Treatment may be delayed until the patient has recovered from drug-induced toxicity. Two courses are required for an adequate trial.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZQ - 10 mg vials.

DATE SUMMARIZED: 01/81

12.0030 ADJUVANT CHEMOTHERAPY WITH CACP/BLEO PLUS SURGERY AND RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) HNCP-178

OBJECTIVES:

I. Compare in patients with operable squamous cell carcinoma of the oral cavity, oropharynx, larynx and hypopharynx the relative efficacies of (a) 'standard' therapy with surgery and postoperative radiation therapy and (b) 'standard' therapy plus preoperative induction chemotherapy with cis-platinum (CACP)/bleomycin (BLEO) and (c) 'standard' therapy preceded by induction chemotherapy and followed by maintenance chemotherapy.

II. Compare the relative toxicities of the three regimens with particular attention to nutritional and performance status of the patient.

III. Determine quantity and quality of tumor response prior to definitive local therapy.

PROTOCOL ENTRY CRITERIA: Patients between 30 and 78 years old with biopsy confirmed resectable Stage II, III or IV M0 squamous cell carcinoma of the oral cavity or larynx/hypopharynx. Patients must not have a history of malignancy nor prior therapy for the present disease. Patients must have adequate hematologic, renal, pulmonary and cardiac status and a performance status of 50 or better.

PROTOCOL OUTLINE: Randomized study. (Initial treatment should begin within 7 days of randomization; delay beyond 14 days constitutes a protocol violation. Addendum 1, July 1979.)

Arm I: Surgery plus Radiotherapy. Cobalt teletherapy or supervoltage.

Arm II: 2-Drug Combination Chemotherapy plus Surgery and Radiotherapy. Cis-Platinum - CACP, NSC-119875; Bleomycin, BLEO, NSC-125066.

Arm III: 2-Drug Combination Chemotherapy plus Surgery and Radiotherapy and Single-agent Maintenance Chemotherapy. CACP; BLEO. Maintenance: CACP.

STRATIFICATION BY: Participating institutions; site of disease: anterior tongue, floor of mouth, retromolar trigone/anterior tonsillar pillar, glottic larynx, supraglottic larynx, pyriform sinus; disease Stage II and III vs. IV.

SPECIAL STUDY PARAMETERS: Audiogram, dental and nutritional evaluation, liver and bone scans.

END POINTS: Objective tumor response prior to definitive local therapy, response/remission rate, survival rate, duration of response, toxicity/morbidity of treatment, recurrence rate, survival time.

CURRENT STATUS: 200 patients will be entered in 2 1/2-3 years.

DOSAGE SCHEDULE:

Arm I: Surgery as indicated. Begin Radiotherapy 3 to 4 or up to 10 weeks postoperative - 5000 to 6000 rad in 5 to 7 1/2 weeks to primary and areas of suspected disease.

Arm II: CACP - 100 mg/sqm iv with hydration and diuresis on day 1; BLEO - 15 mg/sqm rapid iv on day 3, followed by 15 mg/sqm/day iv infusion on days 3 through 7. Perform Surgery in week 4, Radiotherapy 4 to 10 weeks postoperative, as in Arm I.

Arm III: CACP, BLEO as in Arm II, Surgery and Radiotherapy as in Arm I plus Maintenance, begining 4 weeks after Radiotherapy. CACP - 80 mg/sqm/day iv infusion on day 1. Repeat CACP q month for 6 months.

Follow all patients monthly for 1 year, q 2 months for 1 year, then q 3 months for 1 year.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: CACP - 10 mg vials; BLEO - 15 unit/ampules.

DATE SUMMARIZED: 02/79

12.0031 CHEMOTHERAPY WITH CMF-BLEO (BLEO/CTX/MTX/5-FU) WITH OR WITHOUT BCG IMMUNOTHERAPY FOR HIGH-RISK SQUAMOUS-CELL HEAD AND NECK CANCER

Jesse, R. M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-205; MDA-S33/BN20

OBJECTIVES:

I. Determine if addition of chemotherapy or chemoimmunotherapy to conventional treatment can improve length of remission and survival.

II. Determine if immunologic testing can act as a prognostic factor and can be correlated with tumor burden and patient status prior to conventional treatment.

III. Characterize duration and degree of immunosuppression after conventional therapy.

IV. Determine if serial modification of immunotherapy can maintain or restore immunocompetency and in turn maintain patient in remission.

V. Observe and quantitate toxicity.

VI. Search for additional prognostic factors and for incidence of distant metastasis, local recurrence or persistence during conventional therapy.

PROTOCOL ENTRY CRITERIA: Patients with squamous-cell carcinoma of oral cavity, oropharynx, hypopharynx, nasopharynx, larynx and sinuses, staged T3 or 4, or N2, 2b or 3 (patients with lymphoepithelioma of nasopharynx irrespective of T and/or N staging), who are free of gross disease following conventional therapy, and patients with recurrent local or regional squamous-cell carcinoma confined to any head or neck area, any stage, controlled by conventional treatment. Patients in both categories must be less than 75 years of age, have an absolute granulocyte count of at least 2000/cumm and platelet count of at least 100,000/cumm, and live near a medical facility adequate for the administration and maintenance of chemotherapy.

PROTOCOL OUTLINE: Randomized study. Separately randomize Group I (those with squamous-cell carcinoma of oral cavity, oropharynx, hypopharynx, nasopharynx, larynx and sinuses, staged T3 or 4; or N2, 2b or 3 and with any stage lymphoepithelioma of nasopharynx, who are free of gross disease) and Group II (those with recurrent local or regional, any stage, squamous-cell carcinoma confined to the head and neck and controlled by conventional therapy) patients to one of the following arms. Repeat randomization of patients in Arm I should they recur and be rendered free of disease by conventional therapy a second time.

Arm I: No-therapy control group.

Arm II: 4-Drug Combination Chemotherapy. CMF-BLEO: Cyclophosphamide, CTX, NSC-26271; Methotrexate, MTX, NSC-740; 5-Fluorouracil, 5-FU, NSC-19893; Bleomycin, BLEO, NSC-125066.

Arm III: 4-Drug Combination Chemotherapy plus Immunotherapy. Chemotherapy as in Arm II; BCG-Connaught, BCG, NSC-B116341.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 75 patients will be entered per year.

DOSAGE SCHEDULE:

Arm I: No therapy.

Arm II: CTX - 500 mg/sqm iv on day 1; MTX - 40 mg/sqm iv infusion on days 1 and 5; 5-FU - 500 mg/sqm iv on days 1 and 5; BLEO - 30 mg iv infusion on days 1 and 5 for first 3 courses. Continue CMF therapy for one year. Withhold MTX in patients with serum creatinine over 1.5 mg% or clearance less than 60 mg/min; withhold BLEO in patients with vital capacify less than 60% of predicted.

Arm III: Chemotherapy as in Arm II; BCG, route and dosage not given, on days 7, 14 and 21 of each CMF course. Drop patients from study on recurrence.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/77

12.0032 PILOT STUDY OF COMBINATION CHEMOTHERAPY WITH ADRIAMYCIN/CIS-PLATINUM FOR METASTATIC THYROID CARCINOMA

Burgess, M. A., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-262; MDA-DT-7767

OBJECTIVES:

I. Determine the effectiveness of combination chemotherapy with adriamycin (ADR)/cis-platinum (CACP) in patients with metastatic thyroid cancer.

PROTOCOL ENTRY CRITERIA: Patients with metastatic thyroid carcinoma, including papillary, follicular, Hurthle cell, medullary, anaplastic, spindle and giant cell types. Patients must have recovered from toxicities of prior therapies; cases with improved cardiac or renal function must be discussed with study coordinator.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate.

CURRENT STATUS: 10 patients will be entered per year.

DOSAGE SCHEDULE:

ADR - 75 mg/sqm (maximum cumulative dose 550 mg/sqm) iv on day 1; CACP - 75 mg/sqm iv on day 1. Repeat course q 21 days for 2 courses, then evaluate and continue ADR therapy as above for responding or stable patients.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

12.0033 PHASE II CHEMOTHERAPY WITH PCNU FOR REFRACTORY SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) MDAR-395; MDA-DT-8019

OBJECTIVES:

I. Determine the efficacy of PCNU administered by intravenous infusion every 6-8 weeks to patients with recurrent squamous cell carcinoma of the head and neck, including lymphoepithelioma.

II. Determine the qualitative and quantitative toxicity of PCNU administered in this fashion.

III. Determine duration of response and survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven head and neck squamous cell cancer (including lymphoepithelioma), with measurable lesions, who have failed treatment of higher priority. Patients with brain metastasis must concurrently receive whole brain irradiation. Patients must be at least 15 years of age and have a life expectancy of at least 12 weeks and adequate bone marrow, liver, and renal function. Patients must not receive chemotherapy, immunotherapy, or radiotherapy for 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. PCNU, NSC-95466.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic function test, tumor measurements.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response, toxicity/morbidity of treatment, survival.

CURRENT STATUS: A minimum of 30 patients will be entered.

DOSAGE SCHEDULE:

PCNU - 100 mg/sqm iv q 6 to 8 weeks in good-risk patients (adequate bone marrow reserve and no prior treatment with mitomycin-C). Poor-risk patients (inadequate bone marrow reserve, prior mitomycin-C, or extensive prior radiotherapy) receive 60 mg/sqm. Chemotherapy is continued for 2 years or for one year after achieving CR, whichever is shorter.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/80

12.0034 IMMUNOTHERAPY WITH LEVAMISOLE FOR RESECTABLE HEAD AND NECK CANCERS

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PROTOCOL NUMBER(S) MSKCC-7375

OBJECTIVES:

I. Determine the effect of levamisole on immune reactivity of patients with operable head and neck cancer.

II. Reduce the rate of local recurrence and lengthen the disease-free interval after resection of head and neck cancer.

PROTOCOL ENTRY CRITERIA: Patients with operable epidermoid cancer of oral cavity, pharynx, and larynx.

PROTOCOL OUTLINE: Randomized study. Patients randomized following Surgery.

Arm I: Immunotherapy. Levamisole, LEV, NSC-177023.

Arm II: Placebo.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Skin tests: DNCB, commonly injected antigens; in vitro lymphocyte functions: common antigen stimulation, enumeration of T and B cells; immunoglobulin levels in serum.

END POINTS: Disease-free interval, response/remission rate, duration of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: LEV - 150 mg po daily for 3 days q 2 weeks.

Arm II: Placebo.

Patients continue treatment for 1 year or until time of recurrence.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

12.0035 SEQUENTIAL ADDITION/DELETION OF MTX/CF, CACP/BLEO, CTX, 5-FU FOR METASTATIC, OR LOCALLY ADVANCED SQUAMOUS CELL HEAD & NECK CANCER

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PROTOCOL NUMBER(S) SFCC-78068

OBJECTIVES:

I. Develop an effective multimodality approach to advanced squamous cell carcinoma of the head and neck (SCHN) using combination chemotherapy, radiotherapy and surgery.

II. Investigate whether pre-operative or pre-radiotherapy chemotherapy can: (1) prolong the disease free survival, (2) increase the number of patients eligible for curative therapy, (3) increase the incidence of local control, (4) decrease the incidence of distant metastasis.

III. Develop a comprehensive chemotherapeutic and alternate therapy plan for patients with advanced SCHN not eligible for curative procedures.

IV. Design a chemotherapy approach which will allow evaluation of single agent activity in treated and untreated patients using similar evaluation criteria and similar staging information.

V. Design a chemotherapy schema which will allow in vivo correlation with ongoing in vitro studies of tumor sensitivity to antineoplastic agents (Salmon technique experiments of Drs. Lazarus, Kufe, Rhinewald).

VI. Develop a chemotherapy schema which will allow for studies of drug interactions as they correlate to tumor responsiveness or resistance.

VII. Develop an accurate assessment of tumor volume in advanced head and neck tumors.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically confirmed, recurrent, metastatic or locally advanced squamous cell carcinoma of the head and neck, ineligible or failing alternate modes of radiotherapy or surgery. Patients must have recovered from prior therapy and must have a minimum life expectancy of 2 months, a performance status less than 3 and adequate renal, hepatic and hematologic status.

PROTOCOL OUTLINE: Randomized study. Randomize patients eligible for curative therapy to Arm I or V; randomize all others to Arms I, II, III or IV.

Arm I: 6-Drug Sequentially Additive Combination Chemotherapy. Methotrexate, MTX, NSC-740; Citrovorum Factor, CF, NSC-3590; Cis-platinum, CACP, NSC-119875; Bleomycin, BLEO, NSC-125066; Cyclophosphamide, CTX, NSC-26271; 5-Flourouracil, 5-FU, NSC-19893.

Arm II: 6-Drug Sequentially Additive Combination Chemotherapy. CACP, BLEO, MTX, CF, CTX, 5-FU.

Arm III: 6-Drug Sequentially Additive Combination Chemotherapy. CTX, MTX, CF, CACP, BLEO, 5-FU.

Arm IV: 6-Drug Combination Chemotherapy. 5-FU, MTX, CF, CACP, BLEO, CTX.

Arm V: Conventional Surgery or Radiotherapy.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: IVP, liver and renal function, xeroradiography, tomography or ultrasound when indicated.

END POINTS: Response/remission rate, objective tumor response, disease free interval, survival time.

CURRENT STATUS: About 75 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Arm I: MTX - 100 mg/sqm iv on day 1; CF - 50 mg/sqm iv on day 2. Repeat q week for 4 courses. Delete MTX; CF if disease progresses after 4 weeks otherwise give CACP - 20 mg/sqm iv on days 1 through 5; BLEO - 15 U/sqm iv on days 3 through 8; MTX - 100 mg/sqm iv on days 8, 15, and 22; CF - 50 mg/sqm iv on days 9, 16, and 23. Delete CACP; BLEO if disease progresses after 4 weeks, otherwise give MTX, CF, CACP, BLEO as above; plus CTX - 100 mg/sqm po on days 1 through 14. Delete CTX if disease progresses after 4 weeks, otherwise give MTX, CF, CACP, BLEO, CTX as above; plus 5-FU - 600 mg/sqm iv on days 1 and 8. Continue therapy until relapse. Patients for curative therapy can continue in Arm I up to 16 weeks or until disease is stable or progressive, at which time enter patient to conventional therapy with surgery and/or radiation.

Arm II: CACP, BLEO as in Arm I. Delete CACP; BLEO after 4 weeks if disease progresses, otherwise give CACP, BLEO as above; plus MTX - 100 mg/sqm iv on days 8, 15 and 22; CF - 50 mg/sqm iv on days 9, 16 and 23. Delete MTX; CF after 4 weeks if disease progresses, otherwise give CACP, BLEO, MTX, CF as above; CTX as in Arm I. Delete CTX after 4 weeks if disease progresses, otherwise give CACP, BLEO, MTX, CF, CTX as above; 5-FU as in Arm I. Continue therapy until relapse.

Arm III: CTX - 200 mg/sqm po on days 2 through 14. Delete CTX after 4 weeks if disease progresses, otherwise give CTX as above; plus MTX, CF as in Arm I. Delete MTX/CF if disease progresses after 4 weeks, otherwise give CACP, BLEO as above; MTX, CF as in Arm II; CTX as in Arm I; delete CACP/BLEO if disease progresses after 4 weeks, otherwise give CACP, BLEO as above; MTX, CF as in Arm II; CTX and 5-FU as in Arm I. Continue therapy until relapse.

Arm IV: 5-FU - 600 mg/sqm iv on days 1 through 5. Delete 5-FU if disease progresses after 4 weeks, otherwise give 5-FU as above; MTX, CF, as in Arm I. Delete MTX/CF if disease progresses after 4 weeks, otherwise give 5-FU, CACP, BLEO as in Arm I; MTX, CF as in Arm II. Delete CACP/BLEO if disease progresses after 4 weeks otherwise give 5-FU, CACP, BLEO, CTX as in Arm I; MTX, CF as in Arm II. Continue therapy until relapse.

Arm V: Conventional surgery or radiotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

12.0036 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED HEAD AND NECK CANCER

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PROTOCOL NUMBER(S) WSU-C-31179

OBJECTIVES:

I. Determine the efficacy of chemotherapy with AMSA in advanced head and neck cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed, advanced squamous cell carcinoma or adenocarcinoma (adeno-cystic) of the head and neck who are ineligible for or have failed on a first priority protocol. Patients must have measurable lesions that can be clearly defined on liver scans or roentgenograms; serial photographs of flattened or unmeasurable tumors are also acceptable. Patients must have a life expectancy of at least 8 weeks, a performance status of at least 30%, and adequate hematologic and liver function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: SMA-12, reticulocyte count, appropriate x-rays and isotopic scans.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 25 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Poor-risk patients (PRP): Age over 65, WBC 2500-4000, platelets 75,000-99,999, bilirubin between 1.5 and 3.0 mg%, prior extensive radiation to 50% or more of potential marrow areas, or marked intolerance to chemotherapy. AMSA - 120 mg/sqm (100 mg/sqm for PRP) iv over 30 to 60 min q 3 weeks for a minimum of 2 courses. Continue therapy until tumor progression, development of unacceptable toxicity, or decrease in performance status with stable disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 11/79

12.0037 PRESURGICAL AND ADJUVANT CHEMOTHERAPY WITH METHOTREXATE/CIS-PLATINUM FOR ADVANCED CANCER OF THE HEAD AND NECK, STAGES III AND IV

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PROTOCOL NUMBER(S) CCSF-HN-7801

OBJECTIVES:

I. Evaluate the efficacy of preoperative methotrexate (MTX)/cis-platinum (CACP) in Stages III and IV head and neck cancer.

II. Determine the efficacy of postsurgical MTX/CACP in nonresponders.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with a microscopic diagnosis of Stage III and IV keratinizing, nonkeratinizing, small cell, adeno, mucoepidermoid or lymphoepidermoid carcinoma of the oral cavity (lip excluded), oropharynx, larynx, or salivary glands. Patients must have a life expectancy of at least 2 months, and adequate bone marrow, kidney and liver functions.

PROTOCOL OUTLINE: Randomized study for postsurgical Chemotherapy. Presurgical Chemotherapy: Enter all patients. 2-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; cis-Platinum, CACP, NSC-119875.

Surgery: Enter patients with recurrence following complete response to Chemotherapy and patients with partial response, no response or progression.

Radiotherapy: Enter patients with positive nodes and positive postsurgical margins.

Postsurgical Chemotherapy: Randomize all patients following Radiotherapy and/or Surgery to Arm I or II.

Arm I: 2-Drug Combination Chemotherapy. MTX/CACP.

Arm II: No Chemotherapy.

STRATIFICATION BY: Participating institutions; clinical stage: III vs. IV; histological type: keratinizing vs. nonkeratinizing vs. other; primary site: oral cavity vs. larynx vs. salivary gland vs. other.

SPECIAL STUDY PARAMETERS: SMA-12, bone scan, CEA.

END POINTS: Response/remission rate, duration of response, recurrence rate, survival time, objective tumor responses.

CURRENT STATUS: Expect to enter 120-150 patients per year.

DOSAGE SCHEDULE:

Presurgical Chemotherapy: MTX - 50 mg/sqm po on day 1; CACP - 20 mg/sqm iv on day 2. Repeat course q 7 days for 4 weeks. Continue patients with complete remission on Chemotherapy until recurrence.

Surgery: As necessary, of loco-regional disease, usually including radical neck dissection and 1 cm margins.

Radiotherapy: As necessary for patients with postsurgically residual disease.

Postsurgical Chemotherapy:

Arm I: MTX/CACP, as in Presurgical Chemotherapy. Repeat course q 7 days until disease progression.

Arm II: No Chemotherapy.

Follow patients at least monthly until recurrence.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/78

12.0038 STANDARD VS TIME SEQUENTIAL CHEMOTHERAPY WITH MTX VS MTX/CACP FOR METASTATIC OR RECURRENT CANCER OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) CCSF-HN-7802

OBJECTIVES:

I. Compare the response rate, duration of response and survival of patients with head and neck cancer treated with a standard dose and schedule of methotrexate (MTX) versus an equitoxic dose of MTX given in a time sequential schedule.

II. Compare the above response rates, duration of response and survival with those obtained in patients treated with the combination of MTX/cis-platinum (CACP) administered on a time sequential schedule.

PROTOCOL ENTRY CRITERIA: Patients with evaluable, microscopically diagnosed metastatic or recurrent keratinizing, nonkeratinizing, small cell, adeno, mucoepidermoid or lymphoepidermoid carcinoma of the head or neck. Patients must have a minimum life expectancy of two months and adequate hematologic, hepatic and renal status. They must have the ability to take 2,000 ml of fluid per day, and must not have had prior Chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Methotrexate, MTX, NSC-740, standard schedule.

Arm II: Single-agent Chemotherapy. MTX, time-sequential schedule.

Arm III: 2-Drug Combination Chemotherapy. MTX; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions; primary site: oral cavity vs. larynx vs. other; histological type: keratinizing vs. nonkeratinizing vs. other.

SPECIAL STUDY PARAMETERS: SMA-12, CEA, bone scan.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival rate.

CURRENT STATUS: At least 60 patients will be entered per year.

DOSAGE SCHEDULE:

Arm I: MTX - 50 mg/sqm po on day 1 q 7 days.

Arm II: MTX - 25 mg/sqm po on days 1 and 2 (at 0 and 24 hours). Repeat course q 7 days.

Arm III: MTX - 50 mg/sqm po on day 1 (at 0 hours); CACP - 20 mg/sqm iv on day 2 (at 24 hours). Repeat course q 7 days.

Remove patients with progressive disease or irreversible toxicity after 2 weeks. Continue others until disease progression or a minimum of 4 weeks on therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/78

12.0039 IMMUNOTHERAPY WITH BCG ADJUVANT TO RADIOTHERAPY FOR HEAD AND NECK CARCINOMA

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PROTOCOL NUMBER(S) IL-HN-1

OBJECTIVES:

I. Evaluate the effectiveness of immunotherapy with BCG-Tice as an adjuvant to radiation therapy, both for Induction and for Maintenance at monthly intervals, vs. radiotherapy alone for squamous cell carcinoma of the head and neck.

PROTOCOL ENTRY CRITERIA: Male patients with inoperable head and neck carcinoma who are candidates for curative radiation therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus Immunotherapy. BCG-Tice, BCG, NSC-116327.

Arm II: Radiotherapy.

STRATIFICATION BY: Disease stage, site of disease.

SPECIAL STUDY PARAMETERS: Immunocompetence status: skin tests for 4 recall antigens - DNCB, total T, active T, B-cells.

END POINTS: Length of survival, toxicity/morbidity of treatment, disease-free interval.

CURRENT STATUS: 63 patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: 7000-7500 rads minimum dose administered to tumor over period of 7 to 9 weeks; plus BCG vaccination by multiple tine technique, one pretherapy, then once a week for 12 weeks and monthly thereafter.

Arm II: 7000-7500 rads administered as in Arm I.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 1-2 x 10 to the eighth organisms, Tice strain.

Summary as provided by investigator.

DATE SUMMARIZED: 08/80

12.0040 THERAPEUTIC TRIAL OF DINITROFLUOROBENZENE IN SELECTED PATIENTS WITH CANCER OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) MA-HN-1

OBJECTIVES:

I. Evaluate the effect of intralesional sensitization and immune challenge upon tumor mass using the potent contact sensitizing agent dinitrofluorobenzene (DNFB).

II. Study the effect of DNFB upon the host immune system and monitor immune parameters.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven epidermoid or primary oropharyngeal carcinoma, Stage IV.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy. Dinitrofluorobenzene, DNFB, NSC-33519.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Tumor regression; immune response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

DNFB in acetone-olive oil (1 drop) - 2 mg topical application to visible tumor area. Two weeks after sensitization, challenge with DNFB - 50 micrograms, topical application at initial sensitization site.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

12.0041 COMPARATIVE STUDIES OF IMMUNOTHERAPY WITH BCG AND INH, CHEMOTHERAPY WITH MTX, RADIATION, AND SURGERY FOR DISSEMINATED CANCER OF HEAD AND NECK

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PROTOCOL NUMBER(S) MI-HN-1

OBJECTIVES:

I. Compare the remission rate, survival times and cure rates of patients with disseminated head and neck cancer using radiation, surgery, chemotherapy with methotrexate (MTX) and immunotherapy with BCG-Tice (BCG) and isoniazid (INH) in different combinations.

PROTOCOL ENTRY CRITERIA: Any patient with disseminated cancer of the head and neck.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy plus Single-agent Chemotherapy plus Radiotherapy plus Surgery. BCG-Tice, BCG, NSC-116327; Isoniazid, INH, NSC-9659; plus Methotrexate, MTX, NSC-740; Radiation; and Surgery.

Arm II: Immunotherapy plus Single-agent Chemotherapy plus Radiotherapy. BCG; INH; MTX; Radiation.

Arm III: Radiotherapy plus Surgery.

Arm IV: Surgery.

Arm V: Radiotherapy.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be admitted.

DOSAGE SCHEDULE:

Arm I: BCG - 1 ampule weekly for 12 weeks by multipuncture tine technique, divided among 4-5 sites (both axillae and groin areas and neck near operative site), and thereafter every other week for 2 years. When concurrent with Chemotherapy, BCG is given after MTX. INH - 300 mg/day po after MTX dose. MTX - 50 mg/sqm iv at about weekly intervals until signs of toxicity. No information given regarding Radiotherapy or Surgery.

Arm II: BCG; INH; MTX; Radiation, all as in Arm I.

Arm III, IV, and V: No information given regarding Radiotherapy or Surgery.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCG - 2-8 x 10 to the eighth colony-forming units/ampule.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

12.0042 MTX VS HIGH DOSE MTX/CF VS CACP PLUS SURGERY AND/OR RADIATION PLUS MER IMMUNOTHERAPY FOR EPIDERMOID CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) ARG-HN-7703; ARG-HN-7706

OBJECTIVES:

I. Use chemotherapy with methotrexate (MTX) or cis-platinum (CACP) to diminish tumor mass before radical treatment, in order to improve the chances of success of radiation or surgery.

II. Control residual disease with maintenance immunotherapy with MER-BCG (MER).

PROTOCOL ENTRY CRITERIA: Previously untreated patients with histopathologically diagnosed squamous cell carcinoma of the oral cavity, oropharynx or larynx, Stage III or IV MO. Patients must have adequate renal, hepatic and bone marrow function and be a suitable candidate for conventional radical treatment.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arm I, II or III, then enter to Radical Therapy: radiation and/or surgery depending on disease site and stage. Then rerandomize patients to Immunotherapy Arm IV or V.

Induction:

Arm I: Single-agent Chemotherapy. Methotrexate, MTX, NSC-740.

Arm II: 2-Drug Combination Chemotherapy. MTX; Citrovorum Factor, CF, NSC-3590.

Arm III: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Radical Therapy: Cobalt-60 Radiation and/or surgery.

Maintenance:

Arm IV: Single-agent Immunotherapy. MER-BCG, MER, NSC-143769.

Arm V: No treatment.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Laryngoscopy, immunological studies.

END POINTS: Relapse rate, relapse-free interval, survival time.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: MTX - 40 mg/sqm iv on days 1 and 8. Enter patients to Radical Therapy on about day 20.

Arm II: MTX - 1.5 gm/sqm iv 12-hour infusion on day 1 and 2.5 gm/sqm on day 8 with hydration and urine alkalinization; CF - 12 mg/sqm iv for 12 doses 2 hours after MTX on days 1 and 8. Enter patients to Radical Therapy on about day 20.

Arm III: CACP - 50 mg/sqm iv infusion with hydration and diuresis on days 1 and 2. Enter patients to radical therapy on about day 21.

Radical Therapy: a) Surgery is given as the only treatment when excision margins are highly satisfactory and neck nodes are negative. b) Surgery plus Radiotherapy is used when the excision margins are not satisfactory or neck nodes are histologically positive. c) Radiotherapy is used as the only treatment in cases considered inoperable. Radiotherapy doses: 5,500 rads to the primary tumor and lymph nodes areas when given with surgery and 6,000 rads to the same areas when radiation is the only treatment.

Arm IV: MER - 1 mg given as 0.2 mg to each of 5 sites on the back sc in first month followed by 0.5 mg given as 0.1 mg to each of 5 sites q month for 18 months.

Arm V: No therapy.

Remove patients from study at any time if relapse occurs.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/79

12.0043 DOSAGE SCHEDULE FOR INTRA-ARTERIAL CIS-PLATINUM CHEMOTHERAPY FOR EPIDERMOID CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) ARG-OSITC-1006

OBJECTIVES:

I. Evaluate in a sufficient number of patients the therapeutic response to intra-arterially administered cis-diamminedichloroplatinum, to determine adequate dosage and administration frequency (Phase II), and the maximum tolerable dosage (Phase I) at the regional level.

PROTOCOL ENTRY CRITERIA: Patients with at least one measurable lesion of histologically confirmed primary epidermoid cancer of the head and neck, Stages T3 or T4, NO or N with no more than 1 distant metastasis. Patients must not be over 75 years old, and must not have had any prior therapy within 4 weeks. They must have a life expectancy of at least 3 months with a Karnofsky Performance Status of at least 50% and adequate cardiac, hematologic, renal and hepatic function, and adequate hearing ability.

PROTOCOL OUTLINE: Nonrandomized study. Enter cohorts of 15 patients in sequence to Regimen A, then B, then C. Single-agent Chemotherapy.

Regimen A: Cis-Platinum, CACP, NSC-119875; given q 7 days.

Regimen B: CACP, q 10 days.

Regimen C: CACP, q 21 days.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: ECG, hepatogram, thorax x-ray, audiogram and neurologic study, biopsy of residual lesion.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 45 patients will be entered.

DOSAGE SCHEDULE: Begin hydration of patients 12 hours before CACP administration.

Regimen A: CACP - 20 mg/sqm 6-hour iv infusion q 7 days.

Regimen B: CACP - 40 mg/sqm 6-hour iv infusion q 10 days.

Regimen C: CACP - 60 mg/sqm 6-hour iv infusion q 21 days.

Continue treatment until remission of lesions permits use of radical therapy (Surgery or Radiotherapy), or until unacceptable toxicity requires cessation of treatment. If radical therapy is not indicated, continue with systemic Chemotherapy for at least 8 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg ampules.

DATE SUMMARIZED: 06/79

PATIENT ACCRUAL: 00030779

12.0044 COMBINATION CHEMOTHERAPY WITH CACP/MTX/VCR/BLEO VS CTX/MTX/VCR/BLEO FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) BRA-HN-7702

OBJECTIVES:

I. Determine the efficacy of cis-platinum (CACP)/vincristine (VCR)/methotrexate (MTX)/bleomycin (BLEO) in head and neck cancer.

II. Compare the efficacy of this regimen with cyclophosphamide (CTX)/VCR/BLEO.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically diagnosed, advanced squamous cell carcinoma of head and neck, including lymphoepithelioma, previously untreated or not amenable to curative surgery or radiation. Patients must have a minimum life expectancy of 8 weeks and adequate renal and bone marrow function.

PROTOCOL OUTLINE: Randomized study.

Arm I: Induction: 4-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Methotrexate, MTX, NSC-740; Bleomycin, BLEO, NSC-125066.

Arm II: Induction: 4-Drug Combination Chemotherapy. VCR; MTX; BLEO; cis-Platinum, CACP, NSC-119875.

Maintenance: 4-Drug Combination Chemotherapy. CTX; MTX; VCR; BLEO.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Audiogram, IVP.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, relapse rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Induction: CTX - 400 mg/sqm iv on days 1, 10, 24 and 33; MTX - 15 mg/sqm iv or im on days 1, 10, 24 and 33; VCR - 2 mg iv on days 17 and 40; BLEO - 5 mg (maximum cumulative dose 300 mg) iv on days 1 through 10 and 24 through 33, plus 15 mg iv on days 17 and 40.

Arm II: Induction: CACP - 100 mg/sqm iv on days 1 and 24 with hydration and mannitol diuresis. MTX, VCR and BLEO as in Arm I.

Maintenance: Enter patients in partial or complete remission beginning on day 47. VCR - 2 mg iv on day 1; BLEO - 15 mg iv on day 1; CTX - 400 mg/sqm iv on day 8; MTX - 15 mg/sqm iv or im on day 8. Repeat course q 2 weeks. When maximum dose of BLEO is reached, continue therapy with CTX and MTX as above repeated q 2 weeks.

Remove from study patients with renal or unusual, intolerable toxicity or progression after Induction.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: CACP - 10 mg vials; BLEO - 15 mg vials; MTX - 5 and 50 mg vials; VCR - 1 and 5 mg ampules; CTX - 100 and 500 mg ampules.

DATE SUMMARIZED: 12/78

12.0045 CACP/VCR/MTX/BLEO VS CTX/VCR/MTX/BLEO WITH SURGERY AND/OR RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE HEAD OR NECK

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PROTOCOL NUMBER(S) BRA-HN-7801

OBJECTIVES:

I. Determine the efficacy of combination therapy with cis-platinum (CACP)/vincristine (VCR)/methotrexate (MTX)/bleomycin (BLEO) in head and neck cancer.

II. Compare the efficacy of this regimen with cyclophosphamide (CTX)/VCR/MTX/BLEO.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically diagnosed squamous cell carcinoma of head and neck including lymphoepithelioma not amenable to curative surgery or Radiotherapy. Patients must not have had prior Chemotherapy and must have a minimum life expectancy of 8 weeks. Patients must have adequate renal and bone marrow function. Patients must be free of obstructive uropathy.

PROTOCOL OUTLINE: Randomized study.

Arm I: 4-Drug Combination Chemotherapy. Cis-Platinum, CACP, NSC-119875; Methotrexate, MTX, NSC-740; Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066.

Arm II: 4-Drug Combination Chemotherapy. MTX, VCR, BLEO; Cyclophosphamide, CTX, NSC-26271.

Evaluate all patients as operable or inoperable. Enter inoperable patients to Radiotherapy or remove from study. Enter all others to surgery followed by Maintenance.

Radiotherapy as appropriate. No details given.

Maintenance: 4-Drug Combination Chemotherapy. CTX, MTX, VCR; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions, operability, stage of disease.

SPECIAL STUDY PARAMETERS: Audiogram, bone scan, IVP or renal scan.

END POINTS: Objective tumor response, response/remission rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CACP - 80 mg/sqm iv with hydration and mannitol diuresis on day 1; MTX - 15 mg/sqm iv or im on days 1 and 10; BLEO - 5 mg iv on days 1 through 10 and 30 mg (lower to 15 mg for second course) 6 hours after VCR on day 18; VCR - 2 mg iv on day 18. Repeat course q 25 days for 3 courses. Omit VCR and BLEO on day 18 of third course.

Arm II: MTX, VCR, BLEO as in Arm I; CTX - 300 mg/sqm iv on day 1 and 10. Repeat courses as in Arm I.

Surgery: As appropriate.

Maintenance: Enter patients in complete remission (no residual tumor) for 6 courses, patients in partial remission (residual tumor) for 2 courses followed by Radiotherapy, plus 4 more courses of Maintenance. CTX - 300 mg/sqm iv on day 1; VCR - 1 mg iv on day 1; ADR - 50 mg/sqm iv (maximum cumulative dose 500 mg/sqm) on day 1; MTX - 30 mg/sqm iv on day 1. When maximum dose of ADR is reached doses of CTX - 500 mg/sqm, MTX -50 mg/sqm and VCR - 1 mg are used. Repeat course q 28 days.

Radiotherapy as appropriate.

Enter inoperable patients after Radiotherapy with partial remission to Maintenance until disease progression, with complete remission to Maintenance for 1 year. Enter operable patients after Radiotherapy to Maintenance for 1 year. Remove from study nonresponders to Induction or Radiotherapy, patients with progressive disease, renal failure or unacceptable toxicity.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: CACP - 10 mg vials; BLEO - 15 mg vials; MTX - 5 and 50 mg vials; VCR - 1 and 5 mg ampules; CTX - 100 and 500 mg ampules.

DATE SUMMARIZED: 12/78

12.0046 RADIOTHERAPY WITH OR WITHOUT CONCURRENT BLEOMYCIN/CIS-PLATINUM FOR NONRESECTABLE EPIDERMOID CANCER OF THE HEAD & NECK

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PROTOCOL NUMBER(S) BRA-HNI-7902

OBJECTIVES:

I. Assess the efficacy of radiotherapy and simultaneous chemotherapy with bleomycin/cis-platinum in increasing the complete response rate, the disease-free interval, and the survival of patients with unresectable epidermoid carcinoma at certain primary sites in the head and beck.

II. Document the acute and chronic toxicities associated with simultaneous radiation and chemotherapy.

III. Establish a uniform system of patient evaluation, data collection, and data reporting in the two collaborating cancer centers (A.C. Camargo and MSKCC).

PROTOCOL ENTRY CRITERIA: Patients with unresectable, nonmetastatic, previously untreated, histologically confirmed epidermoid carcinoma of the oral cavity, oropharynx, hypopharynx or larynx. Patients must have adequate renal, bone marrow and auditory function and a Karnofsky performance status of 40 or better.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Megavoltage equipment, Co-60 or greater energy.

Arm II: 2-Drug Combination Chemotherapy plus Radiotherapy. Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

STRATIFICATION: Participating institutions; performance status: 60 or less vs. over 60; primary disease site: oral cavity vs. oropharynx vs. laryngopharynx.

SPECIAL STUDY PARAMETERS: Bone and liver scans, 5-prime nucleotidase, pulmonary, renal and hepatic status.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, duration of response, survival tme, disease-free survival.

CURRENT STATUS: 80 patients will be entered in one year.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - 5000 rad in 5 weeks to the primary and regional lymph nodes, plus 2600 rad to areas of originally bulky disease for a total of 7600 rad. Treatment interruption if needed for Grade III disease should be no more than 2 weeks.

Arm II: Radiotherapy - 2000 rad given in 2 weeks, 10 fraction of 200 rad on 5 days/week. BLEO - 10 mg/sqm im on days 1, 3, 5, 8, 10, and 12 just prior to radiation treatments. Repeat radiation and BLEO therapy beginning on days 29 and 57, and on day 85 to bring the total radiation dose to 7600 rad, as in Arm I. CACP - 40 mg/sqm iv given with adequate hydration on days 15, 22, 43 and 71. Follow up all complete responders without further therapy. Patients with less than complete response may be treated by (1) interstitial radiotherapy - Iridium-192 implants delivering 2000 rad in 2 to 3 days, (2) external boost radiation - by electron beam or other suitable modality, or (3) limited excisional surgery for residual disease. Follow up all patients q 4 weeks in the first year, q 8 weeks in the second year and q 12 weeks therafter until disease recurrence.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/79

12.0047 IMMUNOTHERAPY WITH BCG FOR TUMORS OF THE BUCCAL CAVITY

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PROTOCOL NUMBER(S) EORTC-17761

OBJECTIVES:

I. Determine the effectiveness of BCG immunotherapy for certain tumors of the buccal cavity following curative treatment.

PROTOCOL ENTRY CRITERIA: Male patients with epitheliomas of the floor of the mouth or the tongue, including Stages T1, T2, T3 (with the exception of T3 disease with osseous metastases) and Stages N0, N1, N2 and N3 following radiotherapy alone or radiotherapy following surgery.

PROTOCOL OUTLINE: Randomized study. Randomize patients 7 to 15 days following curative surgery or radiotherapy.

Arm I: Active Nonspecific Immunotherapy. Pasteur BCG, BCG, NSC-B116328.

Arm II: Complementary Therapy. Not specified.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Cervical biopsy; liver function tests; radiography of jaw, mandible and lung.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, disease-free interval.

CURRENT STATUS: 210 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BCG - 150 mg (2 ampules) once a week giving one injection in each limb each month using a Heaf gun scarification technique. Begin BCG 15 days following surgery or radiotherapy and continue therapy for 2 years. Delay BCG for 2 months following radiotherapy where there is evidence of N3 adenopathy in order to determine if the adenopathy has been cured. Follow up all patients for life.

Dosage delay for toxicity is specified.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

12.0048 TWICE DAILY FRACTION VS SINGLE DAILY FRACTION RADIOTHERAPY FOR OROPHARYNGEAL CARCINOMA

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PROTOCOL NUMBER(S) EORTC-22791

OBJECTIVES:

I. Determine whether twice daily fractionated irradiation to a total dose of 8050 rads in 7 weeks will increase the local control rate when compared with classical irradiation of 7000 rads in 7 weeks given in one fraction per day.

PROTOCOL ENTRY CRITERIA: Patients with previously untreated epidermoid carcinoma of the oropharynx: clinical stages T2, T3, N0, N1b less than 3 cm, M0 (U.I.C.C.), in one or more of the following sites: tonsil, glosso-tonsillar sulcus, anterior pillar, posterior pillar, soft palate, lingual face of the epiglottis, lateral wall of the pharynx. Patients must not have lesions whose point of origin is the base of the tongue or the posterior wall of the pharynx, T4 lesions, metastasis, a second-primary, prior surgery or prior systematic chemotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Co-60 gamma rays or megavoltage x-rays. Two fractions/day.

Arm II: Radiotherapy. Co-60 gamma rays or megavoltage x-rays. One fraction/day.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Head and neck examination: tumor measurement, lymph node examination; biopsy of tumor; dental evaluation; x-ray studies: chest x-ray, esophagram, bone x-ray where indicated, hepatic scan.

END POINTS: Response/remission rate, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate.

CURRENT STATUS: 100-150 patients will be entered in each arm.

DOSAGE SCHEDULE:

Arm I: Co-60 gamma rays or megavoltage x-rays - 230 rads/day in two equal fractions separated by 4-8 hours, to a total of 8050 rads in 70 fractions over 7 weeks.

Arm II: Co-60 gamma rays or megavoltage x-rays - 200 rads/day for a total of 7000 rads given in 35 fractions 5 days per week over 7 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 10/80

12.0049 LONG-TERM CYCLOPHOSPHAMIDE CHEMOTHERAPY FOLLOWING RADIOTHERAPY FOR ADVANCED NASOPHARYNGEAL CARCINOMA

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PROTOCOL NUMBER(S) EORTC-24761-NPC-1; UICC-77055

OBJECTIVES:

I. Evaluate in a randomized series the effectiveness of long-term chemotherapy with cyclophosphamide for preventing or delaying general diffusion and local or regional recurrence of nasopharyngeal cancer after radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients with nasopharyngeal carcinoma classified T3 or 4, N0N1aN2a M0 and T1, 2, 3 or 4 N1b, 2b or 3 M0 histologically identified according to the Pathologist's Study Group of the EORTC Head and Neck Group. Patients must not have had prior radiation and chemotherapy elsewhere, and must have adequate hematologic, hepatic, renal and cardiovascular functions.

PROTOCOL OUTLINE: Randomized study.

Radiotherapy. Co-60, linear accelerator or other high-energy source. Enter all patients. Randomize responders with complete T and N regression to Arm I or Arm II.

Arm I: Single-agent Chemotherapy. Cyclophosphamide, CTX, NSC-26271.

Arm II: No further therapy.

STRATIFICATION BY: Radical neck dissection vs. complete regresssion of nodes.

SPECIAL STUDY PARAMETERS: EBV studies, liver scintiscan, lymphangiogram.

END POINTS: Objective tumor response, time to recurrence or appearance of metastases, 5-year survival rate, response/remission rate.

CURRENT STATUS: About 100 patients will be entered in about 3.5 years.

DOSAGE SCHEDULE:

Radiotherapy - 6000 to 7000 rads total dose given in 5 to 7 weeks to the primary tumor and to clinically positive cervical nodes, which must receive a minimum of 5000 rads. Evaluate patients after 6 weeks. Randomize patients with complete TN regression to Arms I or II. If complete T regression and incomplete node regression: perform radical neck dissection (RND), then randomize to Arms I or II: if RND is not feasible or is incomplete or if distant metastases appear, or if there is no or incomplete T and N regression, randomize patients for Protocol UICC-77056.

Arm I: Begin 6 weeks after completion of radiotherapy or, if RND is performed, 15 days after surgery. CTX - 1.2 g/sqm iv q 3 weeks for 10 courses. Adjust dosage according to hematologic toxicity. Follow up patients q 2 months for a total of 5 years. Enter patients who develop distant metastases to Protocol UICC-77056.

Arm II: No further therapy.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/78

12.0050 ADRIAMYCIN CHEMOTHERAPY ALONE OR COMBINED WITH VINBLASTINE/BLEOMYCIN FOR METASTATIC CARCINOMA OF THE NASOPHARYNX

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PROTOCOL NUMBER(S) EORTC-24761-NPC-2; UICC-77056

OBJECTIVES:

I. Test successively different schemes of palliative chemotherapy in patients with far advanced nasopharyngeal carcinoma (NPC) (distant metastases or/and local or regional not otherwise treatable recurrences).

II. Compare different drugs and regimens, two by two, in order to select schemes of chemotherapy to be employed as long-term treatment, as alternatives to cyclophosphamide, in possible new trials, after completion of the trial UICC-77055.

PROTOCOL ENTRY CRITERIA: Patients with nasopharyngeal carcinoma presenting with distant metastases and/or with not otherwise treatable local or regional recurrence on protocol UICC-77055, classified all degrees of T and NM1, or M0 with incomplete regression of T or N following radiotherapy, or patients failing on long-term chemotherapy. Histological classification must be according to the Pathologist's Study Group of the EORTC Head and Neck Group. Patients must have adequate renal, hepatic, hematologic and cardiovascular functions.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Adriamycin, ADR, NSC-123127.

Arm II: 3-Drug Combination Chemotherapy. ADR; Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066.

STRATIFICATION BY: Prior therapy or no prior therapy on Protocol EORTC-26761-NPC-1.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, time to appearance of new metastases, disease-free interval, response/remission rate, length of survival.

CURRENT STATUS: About 100 patients will be entered.

DOSAGE SCHEDULE:

Arm I: ADR - 75 mg/sqm (maximum cumulative dose 550 mg/sqm) iv q 4 weeks.

Arm II: ADR - 30 mg/sqm iv; VBL - 6 mg/sqm iv; BLEO - 25 mg/sqm (maximum cumulative dose 250 mg/sqm) iv. Repeat course q 3 weeks.

Evaluate all patients in Arms I and II after 2 courses. Adjust doses according to hematologic toxicity and continue therapy for responders until maximum prudential doses are reached or until disease progression. Patients with progressive disease after 3 courses or later are removed from trial and are treated with methotrexate (dosage not given).

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/78

12.0051 CHEMOTHERAPY WITH VCR/BLEO/MTX PRIOR TO SURGERY AND RADIOTHERAPY FOR ADVANCED EPITHELIOMAS OF THE HYPOPHARYNX (PYRIFORM SINUS)

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PROTOCOL NUMBER(S) EORTC-24771; UICC-77054

OBJECTIVES:

I. Evaluate the efficacy of one cycle of VCR-BLEO-MTX administered prior to the pharyngolaryngectomy followed by postoperative irradiations for advanced epitheliomas of the pyriform sinus.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven squamous cell carcinoma of the pyriform sinus, Stage T3 N0 N1 N3 (except contralateral) without previous treatment. Patients must not be over 70 years of age, be in good general condition, and have adequate hematological, liver, kidney and pulmonary functions.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy plus Surgery plus Radiotherapy. Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066; Methotrexate, MTX, NSC-740; plus pharyngolaryngectomy and neck dissection; plus Radiotherapy: Cobalt-60, linear accelerator or betatron to primary tumor area, neck node chains on both sides, and submaxillary, upper, mid and lower jugular and spinal accessary sites.

Arm II: Surgery and Radiotherapy. As in Arm I.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: A-P laminograms, barium swallow, pulmonary, liver and kidney function tests.

END POINTS: Toxicity/morbidity of treatment, recurrence rate, recurrence site, recurrence delay, incidence of distant metastases, survival time, 2 and 5 year survival rates.

CURRENT STATUS: 152 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: VCR - 1.5 mg/sqm iv on day 1; BLEO - 20 mg/sqm iv 6 hours after VCR administration on day 1; and MTX - 40 mg/sqm/day iv in two divided doses on days 2 and 3 (total dose - 80 mg/sqm). Eight to fifteen days after completion of Chemotherapy perform pharyngolaryngectomy plus neck dissection. Begin Radiotherapy as soon as satisfactory wound healing is obtained and not later than 30 days after Surgery: 5000 rads given in 5 weeks to patients with clear tumor margins and negative nodes; if tumor margins are doubtful and nodes are positive, give 6000 to 6500 rads to tumor area. Give 5500 to 6000 rads to node areas if the node capsule is intact and 6000 to 6500 rads to the node areas if the node capsule is broken. In any case, give no less than 5000 rads administered in 5 to 7 weeks.

Arm II: Surgery and Radiotherapy, as in Arm I.

Follow up all patients 4 weeks after the end of Radiotherapy and then q 3 months.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 04/79

12.0052 PHASE II COMBINATION CHEMOTHERAPY WITH BLEO/CACP/MTX/VCR FOR METASTATIC OR LOCALLY RECURRENT SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) EORTC-24791

OBJECTIVES:

I. Evaluate the antitumor activity of a combination of methotrexate, bleomycin, cis-platinum and vincristine in advanced squamous cell cancer of the head and neck.

II. Evaluate the toxicity of this combination.

PROTOCOL ENTRY CRITERIA: Patients with histologic or cytologic diagnosis of squamous cell carcinoma of the head and neck, with measurable disease. Patients must have no prior chemotherapy with any of the protocol agents; there must be evidence of progressive disease if evaluated lesions are in previously irradiated areas. Patients must be under 75 years of age and have adequate hematologic, renal and hepatic function. They must have a performance status of at least 60, no evidence of obstructive uropathy, and no other malignancies (except skin cancer).

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. Methotrexate, MTX, NSC-740; Bleomycin, BLEO, NSC-125066, cis-Platinum, CACP, NSC-119875; Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurement; chest tomogram; audiogram; hematologic, renal and hepatic function tests.

END POINTS: Response/remission rate, duration of response, disease-free interval, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: A minimum of 66 patients will be entered.

DOSAGE SCHEDULE:

Treatment is given in 21-day cycles. MTX - 40 mg/sqm iv on days 1 and 15; BLEO - 10 mg iv on days 1, 8, and 15 to a total cumulative dose of 400 mg/sqm; CACP - 50 mg/sqm iv on day 4, with prehydration, 40 mg Furosemide iv and 12.5 g Mannitol diuresis; VCR - 2 mg iv on days 1, 8 and 16 to a maximum of 6 doses. MTX and BLEO are given iv or im. Patients remain on study for at least 28 days; then patients with progressive disease, toxicity or relapse after CR or PR go off study. Response is estimated every week.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 50 mg vials; BLEO - 15 mg ampules; CACP - 10 mg vials; VCR - 1 and 5 mg vials.

DATE SUMMARIZED: 10/80

12.0053 PHASE II CHEMOTHERAPY WITH VINDESINE FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) EORTC-24801

OBJECTIVES:

I. Assess the efficacy of continuous infusions of vindesine as a single agent in head and neck carcinoma.

II. Compare tolerability, toxicity and cumulative toxicity with other vinca alkaloids.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven primary or recurrent squamous cell carcinoma of the head and neck, with measurable or evaluable disease, who have failed on regimens of higher priority. Patients must be under 65 years of age and have a life expectancy of at least 6 weeks and a Karnofsky performance status of at least 40. Hematologic, hepatic and renal functions must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic, renal and hepatic function tests.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 14 patients will be entered.

DOSAGE SCHEDULE:

DAVA - 1.0 mg/sqm/day continuous iv infusion (with an infusion pump) through a central venous catheter, for 24 hours, daily for 5 days. Repeat q 3 weeks or as soon as toxicity permits. All patients receive 2 courses of treatment; remitting and stable patients remain on study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DAVA - 10 mg vials.

DATE SUMMARIZED: 10/80

12.0054 IMMUNOTHERAPY WITH BCG FOR HEAD AND NECK TUMORS

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PROTOCOL NUMBER(S) EORTC-7306; FRE-IGR-7306

OBJECTIVES:

I. Determine whether BCG immunotherapy can prolong the duration of survival in patients with otorhinolaryngological tumors.

PROTOCOL ENTRY CRITERIA: Patients with histological diagnosis of epithelioma of the otorhinolaryngological sphere including the larynx, epiglottis, and hypopharynx, who are eligible for laryngectomy or pharyngolaryngectomy. Also include patients with cervical adenopathies.

PROTOCOL OUTLINE: Randomized study. Enter patients as soon as possible in the week following the completion of radiotherapy or surgery.

Arm I: Immunotherapy. Pasteur BCG, BCG, NSC-B116328.

Arm II: Control Group. No Immunotherapy.

Observe patients living in the vicinity of Paris q month, others q 2 months. Upon relapse, patients are treated by conventional therapy.

STRATIFICATION BY: Prior surgery - total or partial laryngectomy or pharyngolaryngectomy; cervical adenopathies.

SPECIAL STUDY PARAMETERS: DNCB skin tests, T and B lymphocyte rosettes.

END POINTS: Response/remission rate, duration of response, survival rate, duration of survival.

CURRENT STATUS: 100 patients will be entered.

DOSAGE SCHEDULE:

Arm I: BCG - 3 ampules per 25 sqm by scarification on each of four limbs q 7 days. Begin one week following completion of radiotherapy or surgery. Continue for 18 months or until there is evidence of recurrence or metastases.

Arm II: Control Group. No Immunotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/77

12.0055 STANDARD VS SEQUENTIAL MTX VS MTX/CACP CHEMOTHERAPY FOR RECURRENT OR METASTATIC CANCER OF THE HEAD AND NECK

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PROTOCOL NUMBER(S) PERU-INEN-7805

OBJECTIVES:

I. Compare the response rate, duration of response and survival of patients with head and neck cancer treated with a standard dose and schedule of methotrexate (MTX) versus and an equitoxic dose of MTX given in a time sequential schedule.

II. Compare the above response rates, duration of response and survival with those obtained in patients treated with the combination of MTX/cis-platinum (CACP) administered on a time sequential schedule.

PROTOCOL ENTRY CRITERIA: Patients with evaluable, microscopically diagnosed keratinizing, nonkeratinizing, small cell, adeno, mucoepidermoid or lymphoepidermoid carcinoma of the head and neck, metastatic or recurrent following surgery or radiotherapy, who are previously untreated by chemotherapy. Patients must have a minimum life expectancy of 2 months, be able to take 2000 ml of fluid per day and have adequate bone marrow, hepatic and renal function.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Methotrexate, MTX, NSC-740; standard schedule.

Arm II: Single-agent Chemotherapy. MTX, sequential schedule.

Arm III: Sequential 2-Drug Combination Chemotherapy. MTX, standard schedule; plus cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Participating institutions; histologic type: keratinizing vs. nonkeratinizing vs. other; primary site: oral cavity vs. larynx vs. other sites.

SPECIAL STUDY PARAMETERS: SMA-12, CEA, bone scan.

END POINTS: Objective tumor response, response/remission rate, duration of response, survival rate.

CURRENT STATUS: 60 patients will be entered per year.

DOSAGE SCHEDULE:

Arm I: MTX - 50 mg/sqm po on day 1 q 7 days.

Arm II: MTX - 25 mg/sqm po on days 1 and 2 q 7 days.

Arm III: MTX - 50 mg/sqm po on day 1; CACP - 20 mg/sqm iv on day 2 q 7 days.

Evaluate patients after 4 weeks or 2 weeks if toxicity appears. Remove from study patients with progressive disease or moderate irreversible toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/78

12.0056 PHASE II MASSIVE FRACTIONATION SPLIT-COURSE RADIOTHERAPY FOR ADVANCED HEAD AND NECK CANCER

Skolyszewski, J., (Krakow 299-00) Instytut Onkologii, Dept. of Radiotherapy, Garncarska 11, 31-115 Krakow, Poland
PROTOCOL NUMBER(S) POL-HN-1

OBJECTIVES:

I. Determine the tumor response and the curability of advanced head and neck cancer in patients who are in poor general condition.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with advanced (Stage III and IV) head and neck cancer, who are elderly, have cardiac or liver or renal failure (i.e., in poor general physical condition) and who do not qualify for surgery or more aggressive radical radiotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Co-60 source.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Length of survival, survival rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 30 patients are being treated as of March 1980; a total of 50 patients will be entered.

DOSAGE SCHEDULE:

Co-60 - 2000 rads in 4-5 fractions over 4-7 days through bilaterally opposed portals. Patients with superficially situated tumors receive the same dose through a single portal. Three courses are given, for a total dose of 6000 rads. Patients with progressive disease go off study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

Summary as provided by investigator.

DATE SUMMARIZED: 10/80

12.0057 PHASE III NEUTRON RADIOTHERAPY VS CO-60 RADIOTHERAPY PLUS CHEMOTHERAPY WITH VCR/BLEO/MTX FOR ADVANCED HEAD AND NECK CARCINOMA

Skolyszewski, J., (Krakow 299-00) Instytut Onkologii, Dept. of Radiotherapy, Garncarska 11, 31-115 Krakow, Poland

PROTOCOL NUMBER(S) POL-HN-2

OBJECTIVES:

I. Determine the efficacy of neutron radiotherapy for advanced head and neck carcinoma.

II. Compare neutron radiotherapy with combined photon radiotherapy and chemotherapy with vincristine/bleomycin/methotrexate.

PROTOCOL ENTRY CRITERIA: Previously untreated patients with advanced adeno- and squamous cell carcinoma of the head and neck.

PROTOCOL OUTLINE: Patients admitted when cyclotron is available enter Regimen A; those admitted when it is not available enter Regimen B.

Regimen A: Radiotherapy. Cyclotron-generated neutrons.

Regimen B: Radiotherapy plus 3-Drug Combination Chemotherapy. Co-60 photon source; plus Vincristine, VCR, NSC-67574; Bleomycin, BLEO, NSC-125066; Methotrexate, MTX, NSC-740.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Local control, length of survival, toxicity of treatment.

CURRENT STATUS: 40 patients are being treated as of March 1980; 80 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: Neutron Therapy - 1320 rads (n, gamma) tumor dose in 20 fractions over 2 weeks.

Regimen B: Co-60 - 2000 rads tumor dose in 10 fractions over 2 weeks. VCR - 2 mg; after 6 hours, BLEO - 30 mg; after 10 hours, MTX - 200 mg iv 24-hour infusion (after MTX, Citrovorum rescue). Chemotherapy is started immediately following Radiotherapy. Regimen is repeated for a total of 3 courses consisting of Radiotherapy and Chemotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

12.0058 PHASE II RADIOTHERAPY WITH ADJUVANT CHEMOTHERAPY WITH METHOTREXATE FOR TRANSITIONAL CELL CARCINOMA AND LYMPHOEPITHELIOMA OF THE PHARYNX

Reinfuss, M., (Krakow 299-00) Instytut Onkologii, Dept. of Radiotherapy, Garncarska 11, 31-115 Krakow, Poland

PROTOCOL NUMBER(S) POL-HN-3

OBJECTIVES:

I. Determine the efficacy and tolerance of adjuvant chemotherapy with methotrexate and radiotherapy in patients with transitional cell carcinoma and lymphoepithelioma of the pharynx (T1-2,N1-3 and T3, N0-3).

PROTOCOL ENTRY CRITERIA: Patients with transitional cell carcinoma and lymphoepithelioma of the pharynx (T1-2,N1-3 and T3, N0-3) who have received no prior therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy plus Adjuvant Single-agent Chemotherapy. Co-60 irradiation plus Methotrexate, MTX, NSC-740.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Length of survival, toxicity of treatment.

CURRENT STATUS: 20-30 patients will be entered.

DOSAGE SCHEDULE:

Co-60 - 10,000 rads: 5000 rad dose in 24 fractions to the primary, 5000 rad dose in 24 fractions to neck nodes. Additional booster fields for a total of 1000-2000 rads are applied if normal tissue tolerance is not exceeded. Patients showing no evidence of disease 4-6 weeks after Radiotherapy receive MTX - 60 mg/sqm iv. Repeat courses q 4 weeks for 1 year. Patients with progressive disease go off study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 10/80

12.0059 CHEMOTHERAPY WITH MTX WITH OR WITHOUT IMMUNOTHERAPY WITH BCG FOR RESIDUAL EPIDERMOID CARCINOMA OF THE HEAD AND NECK IN THE DETECTABLE STAGE

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PROTOCOL NUMBER(S) URU-HN-1

OBJECTIVES:

I. Evaluate remission response of residual epidermoid carcinoma after treatment with chemotherapy of methotrexate (MTX) or combination chemotherapy and immunotherapy of MTX and BCG.

II. Compare the effectiveness of MTX vs. MTX/BCG.

PROTOCOL ENTRY CRITERIA: Patients up to 75 years of age with histologically confirmed epidermoid carcinoma originating in a head or neck organ. Patients must have had prior curative or palliative surgery or radiotherapy and prior treatment for undetectable residual disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Methotrexate, MTX, NSC-740.

Arm II: Single-agent Chemotherapy plus Immunotherapy. MTX plus BCG (M.S.P.-R.O.U.).

STRATIFICATION: Age, disease stage, prior treatment.

SPECIAL STUDY PARAMETERS: Preoperative or initial TNM classification, hepatic function with transaminases, skin tests to evaluate cellular immunity (PPD, DNCB).

END POINTS: Treatment will be regarded as failure if after 6 courses of chemotherapy or chemoimmunotherapy the tumor remains unchanged, has grown, or has undergone less than 25 percent partial remission.

CURRENT STATUS: Twenty-one evaluable patients have been entered as of February 1980.

DOSAGE SCHEDULE:

Arm I: MTX - 10 mg/sqm for 4 days/month (in 2 daily doses if given po). Check for hematological toxicity on 14th day after series. Evaluate remission after 6 courses of treatment. Patients with complete or partial remission will continue on protocol until 12 courses have been completed. At the end of 12 courses patients in complete remission will be checked periodically.

Arm II: MTX - 10 mg/sqm for 4 days/month; plus BCG - 0.1 mg id x 5 inoculations on 15th day after start of series.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 2.5 mg 'drops'; BCG - not given.

Summary as provided by investigator.

DATE SUMMARIZED: 02/80

SECTION 13

BRAIN AND OTHER CNS TUMORS

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SECTION 13

BRAIN AND OTHER CNS TUMORS

13.0001 PHASE II ADJUVANT CHEMOTHERAPY WITH CLZ, TZT, CACP, OR BCNU/5-FU FOR INTRACRANIAL NEOPLASMS

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PROTOCOL NUMBER(S) BTSG-7820

OBJECTIVES:

I. Determine in a patient population with known malignant brain tumor who have undergone cytoreductive surgery and appropriate radiotherapy, the comparative efficacy of treatment with chlorozotocin (CLZ), Baker's antifol (TZT), cis-platinum (CACP) or BCNU/5-fluorouracil (5-FU).

II. Determine the acceptable dose, schedule, and toxicities of new Phase II chemotherapeutic regimens in patients with malignant glioma.

III. Develop a body of knowledge concerning recurrent and late stage brain tumor patients and to determine the possible prognostic and predictive factors which will assist in study design and analysis.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with proven intracranial neoplastic disease. Patients must have adequate hematologic, renal and hepatic function, a performance status above 30, and a minimum life expectancy of 8 weeks. Patients must have concluded prior Chemotherapy at least 2 weeks ago. Patients with cerebral metastases from primarily breast and bronchogenic carcinomas may be separately stratified according to primary cell type.

PROTOCOL OUTLINE: Randomized study. Enter all patients to Surgery and/or Radiotherapy as indicated, then randomize to Arm I, II, III or IV.

Arm I: Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

Arm II: Single-agent Chemotherapy. Baker's Antifol, TZT, NSC-139105.

Arm III: Single-agent Chemotherapy. Cis-Platinum, CACP, NSC-119875.

Arm IV: 2-Drug Combination Chemotherapy. BCNU, NSC-409962; 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Participating institutions; histologic type; performance status: 80 or more vs. 70 or less.

SPECIAL STUDY PARAMETERS: CT scan, arteriograms, pneumoencephalogram, isotopic brain scan, ultrasonic scan.

END POINTS: Survival rate, response/remission rate, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: A minimum of 180 patients will be entered.

DOSAGE SCHEDULE:

Arm I: CLZ - 200 mg/sqm iv on day 1 q 8 weeks.

Arm II: TZT - 500 mg/sqm iv on days 1, 8, 15, 22, 29, 36. Repeat course q 8 weeks.

Arm III: CACP - 50 mg/sqm iv on day 1 q 4 weeks.

Arm IV: BCNU - 200 mg/sqm iv on day 1; 5-FU - 1 gm/sqm iv on days 15 through 17. Repeat course q 8 weeks.

Evaluate patients for treatment failure by progressive disease, increased steroid requirement and by symptomatic relief or neurological deterioration. Patients failing in one Arm may be rerandomized and crossed over to another Arm.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: CLZ - 50 mg vials; TZT - 100 and 250 mg ampules; CACP - 10 mg vials; BCNU - 100 mg ampules 5-FU - 500 mg vials.

DATE SUMMARIZED: 11/78

13.0002 POSTOPERATIVE RADIOTHERAPY AND COMBINATION CHEMOTHERAPY WITH BCNU, PCB, HU, AND VM-26 FOR MALIGNANT GLIOMA

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PROTOCOL NUMBER(S) BTSG-8001

OBJECTIVES:

I. Evaluate the therapeutic efficacy of postoperative radiotherapy plus one of the following chemotherapeutic regimens in patients with malignant glioma: BCNU alone; alternating courses of BCNU and procarbazine (PCB); and alternating courses of BCNU/hydroxyurea (HU) and PCB/VM-26.

PROTOCOL ENTRY CRITERIA: Patients above the age of 15 years who have undergone cytoreductive surgery for supratentorial malignant glioma. Patients must have a Karnofsky performance status of greater than 30 and may not have received prior chemotherapy or radiotherapy for their tumor. There may be no second primary malignancy except for nonmelanomatous skin cancer or cancer of the cervix.

PROTOCOL OUTLINE: Randomized study. Enter all patients to Regimen A and randomize to Arms I, II, or III.

Regimen A: Radiotherapy. Megavoltage equipment.

Arm I: Single-agent Chemotherapy. BCNU, NSC-409962.

Arm II: 2-Drug Combination Chemotherapy. BCNU; alternating with Procarbazine, PCB, NSC-77213.

Arm III: 4-Drug Combination Chemotherapy. BCNU plus Hydroxyurea, HU, NSC-32065; alternating with PCB plus VM-26, NSC-122819.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: CT scans, hematologic parameters, appropriate blood chemistries.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 58 patients will be required for each treatment group.

DOSAGE SCHEDULE:

Regimen A: 6020 rad through opposing bilateral ports to the entire cranial contents over 7 weeks in 5 daily fractions of 172 rad per week. Begin treatment within 3 weeks of surgical resection and in conjunction with Chemotherapy in Arms I-III.

Arm I: BCNU - 80 mg/sqm/day iv over 30-60 minutes on days 1 through 3. During the first course, BCNU will be given approximately 16 hours prior to Radiotherapy treatments. Repeat course at 8-week intervals.

Arm II: BCNU - 80 mg/sqm/day iv over 30-60 minutes on days 1 through 3. During the first course, BCNU will be given approximately 16 hours prior to the first 3 Radiotherapy treatments. Repeat courses q 16 weeks. PCB - 150 mg/sqm/day po in divided doses. Begin 8 weeks after start of BCNU and continue for 28 days. Repeat courses q 16 weeks.

Arm III: BCNU - 80 mg/sqm/day iv over 30-60 minutes on days 1 through 3; HU - 1600 mg/sqm/day po in divided doses q other day beginning on day 4; PCB - 150 mg/sqm/day po in divided doses for 28 days beginning at week 8; VM-26 - 130 mg/sqm/week iv over 1 hour for a total of 6 doses beginning on week 8. During first course, BCNU should be given approximately 16 hours prior to each of the first 3 Radiotherapy treatments. Repeat courses at 16-week intervals. During the retreatment courses, HU should be started at one-half the initial dose.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg ampules; others not given.

DATE SUMMARIZED: 12/80

13.0003 PHASE III RADIOTHERAPY WITH OR WITHOUT VCR/CCNU/PCB/PRED CHEMOTHERAPY FOR MEDULLOBLASTOMAS AND EPENDYMOMAS IN CHILDREN

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PROTOCOL NUMBER(S) CCG-942; RTOG-7502

OBJECTIVES:

I. Determine whether addition of chemotherapy, following surgery and full radiation therapy, for children with medulloblastoma and ependymoma will decrease the incidence of local recurrence, decrease the incidence of metastases, increase the time to recurrence, and increase the survival rate.

II. Document the toxicities attendant on combined chemotherapeutic treatment.

III. Examine the effect of prognostic factors such as age and stage on recurrence.

PROTOCOL ENTRY CRITERIA: Patients previously untreated by chemotherapy, 2 to 16 years of age, with medulloblastoma or ependymoma.

PROTOCOL OUTLINE:

Part I: Randomized study. Enter patients 3 weeks following primary surgery to Arm I, then randomize patients to enter Arm II or Arm III.

Arm I: Total spinal and cranial radiotherapy.

Arm II: Control. No further therapy.

Arm III: Single-agent Chemotherapy given concurrently with Radiotherapy: Vincristine, VCR, NSC-67574, followed by 2-Drug Combination Chemotherapy plus Hormone Therapy. VCR and CCNU, NSC-79037, plus Prednisone, PRED, NSC-10023.

Part II: Nonrandomized study. Enter patients with increasing signs of recurrence or disease progression from Part I, Arm II, to Part II Arms IV and VI and those from Part I, Arm III, to Part II, Arms V and VI.

Arm IV: 3-drug Combination Chemotherapy: VCR, CCNU, plus Procarbazine, PCB, NSC-77213.

Arm V: Single-agent Chemotherapy with PCB.

Arm VI: Additional Radiotherapy. Continue until there is evidence of recurrences and metastases.

STRATIFICATION BY: Histological type, metastatic spread, disease & stage according to Chang criteria, age, sex, participating institutions.

SPECIAL STUDY PARAMETERS: Brain scan; axial tomography; echoencephalogram, arteriogram; myelogram; ventriculogram.

END POINTS: Recurrence rate, recurrence-free interval, response rate, length of survival, toxicity/morbidity of treatment, survival rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Part I:

Arm I: Radiotherapy - 3,500 to 4,000 rad to entire CNS axis, plus 5, 000 to 5,500 rad to posterior fossa over 5 to 8 weeks, plus 5,000 rad to spinal metastases.

Arm II: No chemotherapy.

Arm III: VCR - 1.5 mg/sqm iv (maximum dose 2 mg) q 7 days for 2 weeks concurrent with radiotherapy for 8 weeks. Rest 4 weeks following completion of radiotherapy, then give VCR - 1.5 mg/sqm iv on days 1, 8 and 15 q 6 weeks. CCNU - 100 mg/sqm po on day 1 q 6 weeks. PRED - 40 mg/sqm/day in 3 divided doses for 14 days q 6 weeks for 12 months, then taper as tolerated. Repeat 6-week cycles for a total of 8 courses.

Part II:

Arm IV: Enter patients with disease progression in Arm II at 2 months to one year following completion of Arm I radiotherapy. VCR plus CCNU as in Arm III, plus PCB - 50 mg/sqm/day (60 mg/sqm/day beginning in 3rd cycle) po for 14 days q 6 weeks. Continue chemotherapy for 1 year or until relapse.

Arm V: Enter patients with disease progression in Arm III at 3 months to 1 year following completion of Arm I radiotherapy. PCB only, as in Arm IV.

Arm VI: Enter patients with disease progression 1 year or more following entry to Arm I to radiotherapy in addition to Arm IV or Arm V chemotherapy. Patients in Arm IV receive VCR concurrent with Arm VI radiotherapy. All other chemotherapy is given following Arm VI radiotherapy and 1 week of rest. Over a 4-week period give patients with primary tumor recurrence 3000 rad to posterior fossa, give patients with supra-tentorial relapse 4000 rad to recurrent tumor, and give patients with cord relapse 4000 rad to the involved segment or to the whole cord in case of multiple metastases. Dosage modifications for toxicity are given.

DOSAGE FORMS: VCR - 1 and 5 mg vials; CCNU - 10, 40 and 50 mg capsules; PRED - 5 and 25 mg tablets; PCB - 50 mg capsules.

DATE SUMMARIZED: 09/76

PATIENT ACCRUAL: 01560279

13.0004 PHASE III STUDY OF RADIOTHERAPY WITH VS WITHOUT CHEMOTHERAPY WITH VCR/CCNU/PRED AND PCB FOR CHILDHOOD ASTROCYTOMA

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PROTOCOL NUMBER(S) CCG-943

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with vincristine, CCNU, and prednisone followed by additional chemotherapy with procarbazine upon relapse, in terms of the relapse incidence, time to relapse and survival rates in children with grade III-IV astrocytoma, who have had prior surgery and radiotherapy.

II. Compare this chemotherapeutic regimen with radiotherapy alone followed by chemotherapy with VCR/CCNU/PCB for recurrent or metastatic disease.

PROTOCOL ENTRY CRITERIA: Patients between 2 and 21 years of age inclusive with grade III or IV astrocytoma previously untreated by chemotherapy. Enter patients as soon as practical following biopsy or resection of tumor.

PROTOCOL OUTLINE:

Part A: Randomized study. Treatment of primary tumor following biopsy or resection.

Arm I: Radiotherapy - Cobalt-60 or equivalent energy, to the whole tumor.

Arm II: Radiotherapy plus 2-Drug Combination Chemotherapy and Hormone Therapy. Vincristine, VCR, NSC-67574; CCNU, NSC-79037; Prednisone, PRED, NSC-10023.

Part B: Nonrandomized study. Treatment of recurrent tumor following Part A therapy.

Arm III: Early relapse in Arm I. 3-Drug Combination Chemotherapy. VCR, CCNU plus Procarbazine, PCB, NSC-77213.

Arm IV: Late relapse in Arm I. 3-Drug Combination Chemotherapy plus radiotherapy. Chemotherapy as in Arm III, plus re-irradiation.

Arm V: Early relapse in Arm II. Single-agent Chemotheray. PCB.

Arm VI: Late relapse in Arm II. Single-agent Chemotherapy plus radiotherapy. PCB, plus re-irradiation.

STRATIFICATION BY: Participating institutions; age; sex; site of primary tumor: supratentorial vs. infratentorial; extent of metastases; extent of resection: biopsy, partial or total; histological diagnosis.

SPECIAL STUDY PARAMETERS: CSF studies: pressure, protein, sugar, cytology; head circumference; brain and bone scans; EMI; CAT scan; echoencephalogram; immunological tests.

END POINTS: Relapse rate, time to relapse, survival time, survival rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Part A: Enter all patients within 4 weeks of surgery.

Arm I: Children aged 2-3 years: 4500 rads tumor dose in 28 fractions. Children aged 4-21 years: 5250 rads tumor dose in 28 fractions.

Arm II: Radiotherapy, as in Arm I, plus VCR - 1.5 mg/sqm iv q 7 days for 6 weeks beginning within 4 weeks for diagnosis and continued during radiotherapy. Four weeks after completion of radiotherapy give VCR - 1.5 mg/sqm iv on days 1, 8 and 15 of each 6-week course. CCNU -100 mg/sqm po on day 2 q 6 weeks for 8 courses beginning 4 weeks following completion of radiotherapy. PRED - 40 mg/sqm/day po in 3 divided doses on days 1 through 14 q 6 weeks for 9 courses beginning 4 weeks following completion of radiotherapy. Continue chemotherapy for 8 6-week courses, or until prior recurrence or appearance of metastases.

Part B:

Arm III: Enter patients who relapse within 3 to 12 months after entry to Arm I. Repeat course q 6 weeks for 8 courses. VCR - 1.5 mg/sqm iv on days 1, 8 and 15. CCNU - 100 mg/sqm po on day 2 only. PCB - 50 mg/sqm po on days 1 through 14. Escalate dosage by 20% each course to 100 mg/sqm, then continue at this dosage.

Arm IV: Enter patients who relapse more than 12 months after completion of radiotherapy. Chemotherapy, as in Arm III, following 4 weeks after completion of optional radiotherapy: 3,000 rads or less tumor dose in 15 to 18 fractions. Give VCR - 1.5 mg/sqm iv q 7 days during radiotherapy.

Arm V: Enter patients who relapse within 3 to 12 months after entry to Arm II. PCB - 50 mg/sqm po on days 1 through 14. Repeat course q 6 weeks, increasing dose by 20% each course until 100 mg/sqm is reached, then continue therapy at this dosage for a total of 8 courses.

Arm VI: Enter patients who relapse more than 12 months after entry to Arm II. PCB - 100 mg/sqm po on days 1 through 14 q 6 weeks following 4 weeks after completion of optional radiotherapy, as in Arm IV. Continue therapy for 1 year or to prior recurrence.

Remove patients with a second relapse from study. Follow-up all patients for life or for 5 years if free of disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CCNU - 10, 40 and 100 mg; PRED - 5 mg tablets; PCB -50 mg capsules; VCR - 1 and 5 mg vials.

DATE SUMMARIZED: 10/76

PATIENT ACCRUAL: 00310279

13.0005 PHASE III STUDY OF RADIOTHERAPY PLUS HU/BCNU VS HU/PCB/CCNU/VCR FOR PRIMARY MALIGNANT BRAIN TUMORS

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PROTOCOL NUMBER(S) NCOG-6G61

OBJECTIVES:

I. Compare the effectiveness of radiotherapy plus hydroxyurea (HU) followed by BCNU vs. radiotherapy plus HU followed by CCNU/procarbazine (PCB)/vincristine (VCR) for primary, intracranial, malignant glioma.

PROTOCOL ENTRY CRITERIA: Patients at least 15 years old with biopsy-proven (or with clinical, neurological, and neuroradiological evidence that supports no other diagnoses) primary, intracranial, malignant glioma of the following types: glioblastoma multiforme, grade III and IV astrocytoma, anaplastic astrocytoma, gemistocytic astrocytoma and malignant glioma (not otherwise specified). Patients must have: a life expectancy of at least 8 weeks, BUN no greater than 30 mg% or creatinine no greater than 2 mg% (if both tests are done, the patient is eligible if creatinine does not exceed 2 mg%, regardless of BUN); Wbc of at least 4000 and/or granulocyte count of at least 2000 (if both tests are done, the patient is eligible if the granulocyte count is at least 2000, regardless of wbc); platelet count of at least 125, 000; bilirubin no greater than 1.2 mg% and SGOT and alkaline phosphatase no greater than twice the maximum institution normal. Patients must not have had prior cytotoxic chemotherapy and radiotherapy, and must have a minimal Karnofsky rating of 40% (Addendum August, 1978).

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus Single-agent Chemotherapy followed by Single-agent Chemotherapy. Megavoltage radiation to whole brain; plus Hydroxyurea, HU, NSC-32063; followed by BCNU, NSC-409962.

Arm II: Radiotherapy plus Single-agent Chemotherapy followed by 3-Drug Combination Chemotherapy. Radiotherapy as in Arm I; plus HU; followed by PCV: Procarbazine, PCB, NSC-77213; CCNU, NSC-79037; Vincristine, VCR, NSC-67574.

STRATIFICATION BY: Participating institutions; histologic type; glioblastoma multiforme or grade IV astrocytoma vs. anaplastic astrocytoma, gemistocytic astrocytoma, malignant glioma, grade III astrocytoma, or presumed malignant glioma; Karnofsky status: 40 to 70% vs 80 to 100% (Addendum, August 1978).

SPECIAL STUDY PARAMETERS: Kidney and liver function, neurological examination, radionuclide scan, infusion and non-infusion CAT scan.

END POINTS: Time to disease recurrence or progression, response rate, duration of response, length of survival.

CURRENT STATUS: 200 patients will be entered in 2 years.

DOSAGE SCHEDULE: If possible, begin therapy within 4 weeks of diagnosis. Begin Chemotherapy within 14 days after Radiotherapy plus HU has been completed.

Arm I: 6000 rads in 6 to 7 weeks to whole brain; plus HU - 1600 mg/sqm po given in 4 divided doses q other day during Radiotherapy starting on day 1; followed by BCNU - 200 mg/sqm iv infusion over 35 to 40 minutes on day 1 q 6 to 8 weeks.

Arm II: Radiotherapy plus HU, as in Arm I; followed by PCV: PCB -60 mg/sqm/day po on days 8 through 21; CCNU - 110 mg/sqm po on day 1; VCR - 1.4 mg/sqm/day iv push on days 8 and 29. Repeat course q 6 to 8 weeks.

Continue therapy for 2 years unless disease progresses after 3 months have elapsed since the end of Radiotherapy, or until at least 2 courses of Chemotherapy have been given.

Follow up all patients until death.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: PCB - 50 mg capsules; BCNU - 100 mg vials; VCR - 1 mg and 5 mg ampules; HU - 250 and 500 mg capsules; CCNU - not given.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00150378

13.0006 WHOLE BRAIN PHOTON RADIOTHERAPY WITH A PHOTON BOOST VERSUS A NEUTRON BOOST FOR MALIGNANT GLIOMAS

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PROTOCOL NUMBER(S) RTOG-7611

OBJECTIVES:

I. Determine the survival rates using whole brain photon radiotherapy.

II. Determine the interval to symptomatic recurrence

III. Establish the tolerance of the normal brain to a neutron boost vs. a photon boost following whole brain irradiation using photons.

PROTOCOL ENTRY CRITERIA: Patients, over 16 years of age, with histologically proven malignant glioma Grades III or IV. Patients must not have prior chemotherapy, or radiation therapy to the cranium or head and neck region or have metastasis in spinal cord and distant sites, or previous cancer except for small skin cancers outside of the cranial region.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Whole brain photon irradiation plus a photon boost.

Arm II: Radiotherapy. Whole brain photon irradiation plus a neutron boost.

STRATIFICATION BY: Participating institutions, histologic grade of tumor.

SPECIAL STUDY PARAMETERS: EEG, fundoscopic and opthalmological exam, CAT scan, angiography.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response, length and rate of survival, recurrence rate.

CURRENT STATUS: Accrual goal met by June 1980.

DOSAGE SCHEDULE:

For all photon radiation: megavoltage equipment, Cobalt-60 or 2 MeV or greater.

Arm I: Whole brain photon irradiation - total 5000 rads in 5 to 5 1/2 weeks (180 to 200 rad daily fractions, 5 fractions/week). Photon boost - a coned-down boost of 1500 rads given in 8 to 10 fractions in 1 1/2 to 2 weeks.

Arm II: Whole brain photon irradiation - same as in Arm I. Neutron boost - a coned-down boost using neutrons in a dose equivalent to 1500 rads in 6 to 8 fractions given in 1 1/2 to 2 weeks.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/76

PATIENT ACCRUAL: 00280578

13.0007 PILOT STUDY OF RADIOTHERAPY PLUS CCNU CHEMOTHERAPY FOR BRAIN METASTASES

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United States of America

PROTOCOL NUMBER(S) RTOG-7623

OBJECTIVES:

I. Study the effectiveness of CCNU added to the 'best radiotherapy' regime of 3000 rads in 10 fractions.

II. Determine the level of sensitivity of specific tumor types to this radiotherapy and drug combination.

PROTOCOL ENTRY CRITERIA: Patients referred to Radiology Department with brain metastases, with the primary tumor being treated or under control, and a life expectancy of more than 8 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy plus Single-agent Chemotherapy. Supervoltage irradiation to the whole head, plus CCNU, NSC-79037.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Isotopic brain scan, CAT scan, bone scan, LFT, liver scan.

END POINTS: Response rate, recurrence rate, toxicity/morbidity of treatment.

CURRENT STATUS: 15 to 25 patients will be entered.

DOSAGE SCHEDULE:

Treat both parallel opposed fields each day. 3000 rads, given in 2 weeks. CCNU - 18 mg/sqm/day po given 16 to 22 hours before each radiation treatment. Evaluate patient q 6 weeks. Evaluate recurrence 3 months after the end of Radiotherapy.

Dosage modifications for patients with compromised bone marrow are given.

DOSAGE FORMS: CCNU - 10, 40 and 100 mg capsules.

DATE SUMMARIZED: 05/78

13.0008 PILOT STUDY OF CHEMOTHERAPY WITH PULSED DOSES OF BCNU PLUS HIGH-DOSE RADIOTHERAPY FOR MALIGNANT GLIOMA

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PROTOCOL NUMBER(S) RTOG-7701

OBJECTIVES:

I. Compare the survival rate and relapse-free interval achieved by high-dose radiation therapy plus weekly BCNU chemotherapy.

II. Establish the incidence of brain complications following irradiation with and without chemotherapy.

III. Pilot study the administration of BCNU twice weekly during high-dose radiation therapy.

PROTOCOL ENTRY CRITERIA: Patients under 70 years old with histopathologically confirmed malignant glioma Grades III and IV, located supratentorially, and diagnosed by complete or incomplete surgical removal of the glioma. Patients must have adequate postoperative bone marrow, renal and hepatic functions, and adequate blood counts. Patients must not have had prior chemotherapy or immunotherapy or radiotherapy to the cranium or head and neck region. Patients must be presently free of metastatic disease in the spinal cord and distant sites.

PROTOCOL OUTLINE: Nonrandomized study.

Supervoltage Radiotherapy plus Single-agent Chemotherapy. BCNU, NSC-409962.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Renal and liver function tests, brain or CAT scan, EEG, angiography, ECHO or EMI scans, pneumoencephalogram.

END POINTS: Response/remission rate, relapse-free interval, toxicity/morbidity of treatment, survival rate, objective tumor response, quality of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Begin within 4 weeks of Surgery. Radiotherapy: 6000 rads to the whole brain given in 6 to 7 weeks followed by 1000 rad booster given to target volume in 5-7 days. Chemotherapy: BCNU - 20 mg/sqm iv given twice weekly, 16-22 hours prior to next radiation treatment for a total of 12 courses (240 mg/sqm). Give no Chemotherapy while the booster field is applied.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials.

DATE SUMMARIZED: 07/78

13.0009 PHASE II THERAPY WITH MISONIDAZOLE PRIOR TO NEUTRON RADIOTHERAPY FOR GRADE III OR IV SUPRATENTORIAL GLIOMA

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925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) RTOG-7903

OBJECTIVES:

I. Lay the basis for a randomized Phase III study of misonidazole (MNI) and neutron radiation versus misonidazole and photon radiation.

II. Determine the tolerance of the unusual radiation fraction scheme proposed in this protocol in terms of acute and late normal tissue reaction and damage.

III. Establish that the tumor clearance rate, disease-free interval and local tumor control rate are within the expected ranges for malignant gliomas.

PROTOCOL ENTRY CRITERIA: Patients between 18 and 70 years of age with histologically confirmed Grade III or IV supratentorial malignant glioma. Patients must have a Karnofsky performance status of 50% or greater, functional Class I, II or III, and a minimum life expectancy of 4 months. Patients must have adequate renal, neurologic and metabolic status and no prior radiotherapy to the brain nor prior or concurrent chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037; plus neutron radiation to entire cranium.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: CT brain scan, echogram, cerebral arteriography, ventriculogram, pneumoencephalogram.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, relapse-free interval, survival time.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

MNI - 2.5 gm/sqm q 7 days (maximum cumulative dose 15 gm/sqm) po 4 to 6 hours prior to each radiation treatment. Radiation (as amended, May 1980) - 300 neutron rad to the entire brain in single weekly fractions for 4 weeks, plus two 300-rad boost fractions to a reduced volume; total dose - 1200 rad whole brain plus 600 rad boost.

Follow up all patients after 3 weeks, at the end of Radiotherapy, then q 3 months until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MNI - 500 and 100 mg capsules.

DATE SUMMARIZED: 11/79

13.0010 PHASE III MISONIDAZOLE RADIOSENSITIZATION BEFORE RADIOTHERAPY VS RADIOTHERAPY ALONE FOR BRAIN METASTASES

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PROTOCOL NUMBER(S) RTOG-7916

OBJECTIVES:

I. Compare the best standard treatment of brain metastases found from prior RTOG studies to that same fractionation with misonidazole (MNI) against a new fractionation schedule with and without misonidazole for: improvement of neurological functions, time to progression of neurological function or dysfunction, tumor clearance rate and regrowth, proportion of patients requiring treatment of brain metastases, survival and death rate from brain metastases.

II. Determine whether MNI has any effect on response and if it does, whether large fraction high-dose MNI is better than, equal to, or worse than smaller fraction low-dose MNI.

PROTOCOL ENTRY CRITERIA: Patients 18 years to 75 years of age with a histological diagnosis of primary malignancy of any site or histology except lymphoma or leukemias with brain metastases measurable by CT scan. Patients must have multiple metastatic sites, a Karnofsky performance status of 40% or more, neurologic functional classification of I, II, or III and adequate bone marrow, hematologic, renal and liver function. Patients receiving chemotherapy must have no change in such treatment within 2 weeks prior to or during present therapy, nor within 2 weeks following radiotherapy although chemotherapy may be stopped prior to radiotherapy. Patients may not receive concurrent vincristine, vinblastine or cis-platinum.

PROTOCOL OUTLINE: Randomized study. Electron, particle or implant boost radiotherapy is not permitted. Give all patients Hormone Therapy with Dexamethasone, DM, NSC-34521 concurrent with radiation treatment.

Arm I: Radiotherapy. Megavoltage: Cobalt-60 to 8 MeV. 10-fraction schedule.

Arm II: Radiotherapy. 6-fraction schedule.

Arm III: Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037 followed by 10 fractions of Radiotherapy.

Arm IV: Radiosensitization plus Radiotherapy. MNI, as in Arm III, plus 6 fractions of Radiotherapy.

STRATIFICATION: Karnofsky performance status: ambulatory (70 or above) vs. non-ambulatory (40 to 60); neurological function: I or II vs. III; extent of metastases: brain only vs. brain plus other sites.

SPECIAL STUDY PARAMETERS: CT scan; liver function tests, neurological classification.

END POINTS: Response/remission rate, disease-free interval, recurrence rate, survival rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 800 patients will be entered in about 2.5 years.

DOSAGE SCHEDULE:

Arm I: Whole brain radiation - 300-rad fractions, 5 fractions/week for a total of 3000 rad in 2 weeks.

Arm II: Whole brain radiation - 500-rad fractions, 2 fractions/week for a total of 3000 rad in 3 weeks.

Arm III: MNI - 2 g/sqm (total dose 12 g/sqm) given po 4 to 6 hours before Radiotherapy as in Arm I.

Arm IV: MNI - 1 g/sqm (total dose 10 g/sqm) given po 4 to 6 hours before Radiotherapy, as in Arm II.

Give DM - 8 mg/day or greater in 4 divided doses during radiation. Minimum radiation dose rate at the mid-plane in the brain on the central axis must be 50 rad/minute. Use opposed lateral portals to cover entire cranial contents. Remove from study patients too ill to complete treatments or those developing unacceptable toxicity. Follow up all patients with CT scans.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 11/79

13.0011 PHASE III CHEMOTHERAPY WITH BCNU PLUS RADIOTHERAPY WITH OR WITHOUT MNI FOR MALIGNANT GLIOMA

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7918

OBJECTIVES:

I. Determine the survival rate and relapse-free interval in patients treated with misonidazole (MNI)-radiosensitized irradiation plus BCNU vs. standard radiotherapy plus BCNU.

II. Establish the incidence of any increased toxicities or brain complications when MNI-radiosensitized irradiation is combined with BCNU.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven nonrecurrent malignant, supratentorial glioma. Patients must have a minimum life expectancy of 8 weeks, a Karnofsky performance status of 40 or better and adequate hematologic, renal, hepatic and neurologic function. Patients must be between 18 and 70 years old with no prior radiotherapy to the head or neck, or chemotherapy or radiosensitizer therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy plus Radiotherapy. BCNU, NSC-409962; Radiotherapy with megavoltage equipment to the whole brain.

Arm II: Single-agent Chemotherapy plus Radiosensitization plus Radiotherapy. BCNU; Misonidazole, MNI, NSC-261037; Radiotherapy as in Arm I.

STRATIFICATION: Participating institutions; age: 18-44 vs. 45-55 vs. 56-70; performance status: 40-70 vs. 80-100; histology: astrocytoma with foci of anaplasia vs. glioblastoma multiforme.

SPECIAL STUDY PARAMETERS: SMA-12, brain scan.

END POINTS: Response/remission rate, relapse-free interval, survival duration.

CURRENT STATUS: 200 patients to be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: BCNU - 80 mg/sqm iv on days 3 through 5. Repeat q 8 weeks beginning on day 64. Continue for 2 years. Radiotherapy - 6000 rad in 6 to 7 weeks to the whole brain.

Arm II: BCNU as in Arm I. MNI - 2.5 g/sqm po 4 to 6 hours before Radiotherapy on day 1. Repeat q 7 days for 6 courses. Radiotherapy - 400 rad on Monday, 150 rad on Tuesday, Thursday and Friday. Repeat q week for 6 courses then 900 rad in 1 week to whole brain.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 02/80

13.0012 PHASE II NEUTRON/PHOTON MIXED-BEAM RADIOTHERAPY FOR ANAPLASTIC ASTROCYTOMA AND GLIOBLASTOMA

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PROTOCOL NUMBER(S) RTOG-8007

OBJECTIVES:

I. Determine survival rates and interval to symptomatic recurrence following mixed-beam radiotherapy in patients with anaplastic astrocytoma or glioblastoma.

II. Assess the radiation toxicity and establish the tolerance of normal benign tissue to mixed beam (neutron/photon) irradiation and possibly establish a neutron RBE for brain tissue.

PROTOCOL ENTRY CRITERIA: Patients at least 16 years of age with histopathologically confirmed malignant glioma, anaplastic astrocytoma, or glioblastoma; the tumor must be supratentorial. No prior radiotherapy or chemotherapy to cranium or head and neck region may have been given. There must be no major neurologic deficit or psychiatric impairment that would prevent completion of protocol studies, nor any metastases in spinal cord or distant sites.

PROTOCOL OUTLINE: Study partially randomized. Photon irradiation is nonrandomized; patients randomized to one of three doses of fast neutrons.

Mixed-beam Radiotherapy. Photon irradiation (1-10 MeV) to the whole brain plus fast neutrons to the primary tumor.

STRATIFICATION BY: Participating institutions, histologic grade of tumor.

SPECIAL STUDY PARAMETERS: Neurological examination, skull and chest x-ray, ophthalmological examination, CAT scan, angiography, echogram, cerebral air/arteriography studies, funduscopy.

END POINTS: Disease-free interval, recurrence rate, toxicity/morbidity of treatment, survival rate.

CURRENT STATUS: 50-60 patients will be entered in 1.5 years.

DOSAGE SCHEDULE:

Photon irradiation - 4500 rads to whole brain in 30 fractions (150 rads/day, 5 days/week for 6 weeks). Neutron irradiation - 360, 420, or 480 rads (as randomized) to primary tumor only in 12 fractions (2 days/week for 6 weeks), given prior to and within 3 hours of the photon irradiation for that day.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 12/80

13.0013 PHASE III CHEMOTHERAPY WITH MOPP (NM/VCR/PCB/PRED) VS OPP (VCR/PCB/PRED) FOR RECURRENT BRAIN TUMORS IN CHILDREN

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7621

OBJECTIVES:

I. Determine response rate to combination chemotherapy with nitrogen mustard, vincristine, procarbazine and prednisone (MOPP) or vincristine, procarbazine and prednisone (OPP) in children with recurrent brain tumors.

II. Compare response rates to MOPP vs. OPP chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients, 18 years of age or under, who have a central nervous system tumor and who have previously received maximally allowable dose of radiotherapy. Patients must not have received prior therapy with procarbazine. Include medulloblastoma, ependymoma, gliomas, astrocytoma Grade III and IV, oligodendrogliomas, and glioblastoma multiforme, and others.

PROTOCOL OUTLINE: Randomized study.

Arm I: 3-Drug Combination Chemotherapy and Hormone Therapy. MOPP: Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; Prednisone, PRED, NSC-10023.

Arm II: 2-Drug Combination Chemotherapy and Hormone Therapy. OPP: VCR; PCB; PRED.

STRATIFICATION BY: Participating institutions, tumor type.

SPECIAL STUDY PARAMETERS: CAT scan.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective or subjective tumor response.

CURRENT STATUS: 60 patients per year will be entered.

DOSAGE SCHEDULE:

Arm I: MOPP: NM - 6 mg/sqm, iv, on days 1 and 8; VCR - 1.4 mg/sqm (maximum 2 mg), iv, on days 1 and 8; PCB - 50 mg/sqm, po, on day 1, 100 mg/sqm, po, on day 2, and 100 mg/sqm, po, on days 3 through 10; PRED - 40 mg/sqm on days 1 through 10, tapered off over the following 3 days.

Arm II: OPP: VCR, PCB and PRED - dosage schedule as in Arm I.

Repeat courses of both arms q 4 weeks. Adequate trial requires minimum of two courses. Discontinue therapy at evidence of disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: NM - 10 mg vials; VCR - 1 and 5 mg vials; PCB - 50 mg capsules; PRED - 5 mg tablets.

DATE SUMMARIZED: 01/77

PATIENT ACCRUAL: 00450179

13.0014 PHASE III RADIOTHERAPY, DEXAMETHASONE THERAPY, AND CHEMOTHERAPY WITH BCNU, DTIC OR PROCARBAZINE FOR MALIGNANT GLIOMA OF THE BRAIN

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PROTOCOL NUMBER(S) SWOG-7703

OBJECTIVES:

I. Compare the effectiveness of radiotherapy plus BCNU, DTIC or procarbazine for remission induction, duration of remission and survival in patients with malignant gliomas of the brain.

PROTOCOL ENTRY CRITERIA: Patients with primary astrocytoma Grades 3 and 4 who have had surgery with histological diagnosis within 4 weeks of entry, who have had no radiotherapy to the brain, and no chemotherapy other than corticosteroids.

PROTOCOL OUTLINE: Randomized study. All patients are concurrently treated on Regimen A.

Regimen A: Corticosteroid Therapy. Dexamethasone, DM, NSC-34521.

Arm I: Radiotherapy plus Single-agent Chemotherapy. Megavoltage radiation to the entire brain or area of original gross tumor volume; BCNU, NSC-409962.

Arm II: Radiotherapy plus Single-agent Chemotherapy. Radiotherapy as in Arm I; Procarbazine, PCB, NSC-77213.

Arm III: Radiotherapy plus Single-agent Chemotherapy. Radiotherapy as in Arm I; DTIC, NSC-45388.

STRATIFICATION BY: Participating institutions, age, degree of resection.

SPECIAL STUDY PARAMETERS: Psychometric evaluation, brain scan or computerized tomography.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, survival rate, length of survival.

CURRENT STATUS: 210 patients will be entered over 2 1/2 years.

DOSAGE SCHEDULE:

Regimen A: DM - 10 mg/sqm/day po, iv or im for the first 4 weeks of Radiotherapy, then taper to discontinue over 2 additional weeks.

Arm I: Radiotherapy - 6000 rads over 7 weeks; BCNU - 80 mg/sqm/day iv infusion for 3 days beginning 2 days prior to onset of Radiotherapy. Repeat Chemotherapy q 6 weeks hematologic status permitting.

Arm II: Radiotherapy as in Arm I; PCB - 50 mg po on day 1, 100 mg po on day 2 and q day thereafter in 3 or 4 divided doses, beginning 2 days prior to onset of Radiotherapy.

Arm III: Radiotherapy as in Arm I; DTIC - 175 mg/sqm/day iv on days 1 through 5 beginning 2 days prior to onset of Radiotherapy. Repeat course q 4 weeks. Discontinue treatment after 3 months if patient progresses on a myelosuppressive dose. Continue responders to relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; PCB - 50 mg capsules; DTIC - 100 and 200 mg vials; DM - not given.

DATE SUMMARIZED: 01/79

PATIENT ACCRUAL: 00400278

13.0015 RADIOTHERAPY ALONE VS RADIOTHERAPY PLUS FLAGYL FOR TREATMENT OF BRAIN METASTASES

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PROTOCOL NUMBER(S) SWOG-7811

OBJECTIVES:

I. Determine the effectiveness of combined radiation therapy and flagyl in the treatment of patients with brain metastases from primary malignancies outside the central nervous system, compared with radiation therapy alone, as determined by objective response (brain and/or CAT scan) and/or increase in functional neurologic level and duration of response.

II. Determine the toxicity of multiple dose administration of flagyl and radiation therapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven primary malignancy with suspected brain metastases measurable by brain scan, CAT scan or neurologic status level 2 through 4. Patients must have a minimum expected life span of 1 month and may not have had prior radiotherapy to the brain. Patients may not have concurrent chemotherapy with agents known to pass the blood-brain barrier, and must have been removed from such therapy for specified time, unless they failed an adequate trial with any of these agents.

PROTOCOL OUTLINE: Randomized study. Enter all patients to Regimen A; randomize patients to Arm I or II.

Regimen A: Single-agent Hormone Therapy. Dexamethasone, DM, NSC-34521.

Arm I: Radiosensitization plus Radiotherapy. Flagyl, Metronidazole, NSC-69587; plus Radiotherapy, Co-60 or megavoltage.

Arm II: Radiotherapy. Co-60 or megavoltage.

STRATIFICATION BY: Site of primary cancer: breast and lung vs. other; concomitant chemotherapy; initial neurologic status: 1, 2 vs. 3, 4; measurability of intracranial disease; extent of metastases: brain alone vs. brain and other; participating institutions.

SPECIAL STUDY PARAMETERS: Neurologic function, performance status, hepatic, renal function, brain or CAT scan.

END POINTS: Duration of response, survival rate, objective tumor response, response rate.

CURRENT STATUS: 152 patients will be entered within 2 years.

DOSAGE SCHEDULE:

Regimen A: Give concurrently with Arm I or II therapy. DM - 10 mg/sqm/day po in divided doses for 2 weeks, then taper to discontinue.

Arm I: Flagyl - 6 gm/sqm (maximum dose 10 gm) po beginning 2-4 hours prior to Radiotherapy on day 1, then q other day prior to Radiotherapy for a total of 5 doses. Radiotherapy - 3000 rad to entire intracranial content over 2 weeks.

Arm II: Radiotherapy as in Arm I. Remove from study patients with unacceptable stable disease 2 weeks post-Radiotherapy or with progressive disease after 2 weeks of Radiotherapy.

Follow up all patients for life.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Metronidazole - 250 mg tablets; DM - 0.5, 0.75, 1.5 and 4 mg tablets.

DATE SUMMARIZED: 10/78

PATIENT ACCRUAL: 00130179

13.0016 CHEMOTHERAPY WITH ANGUIDINE IN CNS TUMORS

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PROTOCOL NUMBER(S) SWOG-7812; MDAR-292

OBJECTIVES:

I. Determine the antitumor activity of anguidine in the treatment of malignant gliomas relative to clinical response and survival.

II. Observe for expected and unexpected adverse effects and for factors important in producing these effects.

III. Determine the antitumor activity of anguidine in the treatment of malignant brain tumors in children and adolescents relative to clinical response and survival.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed primary CNS tumors: astrocytoma, Grades III and IV; ependymoma; oligodendroglioma; medulloblastoma, or patients under 21 years of age with recurrent brain stem glioma. They must have a life expectancy of at least 8 weeks, granulocyte counts over 2000, platelet counts at least 100,000 and a lesion measurable by scan. They must not have had radiation or chemotherapy for at least 3 weeks. Serum creatinine must not exceed 2.5 mg, nor bilirubin 6.0 mg. (Protocol closed to adults in February 1980 and replaced, for adults, by SWOG-7980.)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Anguidine, ANG, NSC-141537.

STRATIFICATION BY: Participating institutions; poor vs. good risk; astrocytoma vs. other type tumors.

SPECIAL STUDY PARAMETERS: Brain scan or CAT scan.

END POINTS: Response rate, survival time, objective tumor response.

CURRENT STATUS: A minimum of 14 patients will be entered in each stratification.

DOSAGE SCHEDULE:

ANG - 3.5 mg/sqm iv once a week for poor-risk patients (over 65 years of age, poor tolerance of prior chemotherapy; creatinine over 2.0, bilirubin between 3.0 and 6.0 mg percent, elevated hepatic enzymes). Repeat once a week for 4 courses, then increase to 4.5 mg for 4 courses, then to 5.5 mg if toxicity permits. Begin with 5.0 mg/sqm for good-risk patients, increasing to 5.5 and 6.0 as above if possible. Repeat therapy for at least 8 courses. Dexamethsone may be given if required. Remove from study patients with increasing disease after 8 courses, patients who relapse after initial response, or patients with unacceptable toxicity or status quo.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ANG - 5 mg vials.

DATE SUMMARIZED: 10/78

PATIENT ACCRUAL: 00030179

13.0017 PHASE III EVALUATION OF MOPP CHEMOTHERAPY IN THE TREATMENT OF LOCALIZED MEDULLOBLASTOMA AND EPENDYMOMA IN CHILDREN

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PROTOCOL NUMBER(S) SWOG-7909; MDAR-387

OBJECTIVES:

I. Evaluate the efficacy of MOPP: nitrogen mustard (NM), vincristine (VCR), procarbazine (PCB), prednisone (PRED) adjuvant chemotherapy in the prevention of local recurrence of distant metastasis in children with localized medulloblastoma and ependymoma.

II. Evaluate the toxicity of MOPP adjuvant chemotherapy.

III. Evaluate the value of certain prognostic features of medulloblastoma and ependymoma, including age of patient (younger than 5 years versus older at time of diagnosis, presence or absence of spinal cord disease, and type of surgery performed, as well as size of tumor at the time of diagnosis.

IV. Evaluate the different kinds of histopathology of medulloblastoma and ependymoma in children.

V. Evaluate the use of repeated CAT scans in detecting early recurrence of medulloblastoma and ependymoma. Document long-term side effects of radiation therapy and MOPP chemotherapy in children with brain tumors.

PROTOCOL ENTRY CRITERIA: Patients between 1 and 21 (inclusive) with histologically proven medulloblastoma and ependymoma, and registered within 3 weeks after surgery. Patients may have had no antitumor chemotherapy (with exception of corticosteroids), and there may be no metastases outside the CNS.

PROTOCOL OUTLINE: Patients are randomized to Arms I and II following treatment on Regimen A.

Regimen A: Surgery plus Radiotherapy. Excision of tumor where possible plus whole brain irradiation and irradiation of the spinal subarachnoid space with megavoltage equipment (Co-60, 2 MeV x-rays or higher).

Arm I: 3-Drug Combination Chemotherapy plus Hormone Therapy. MOPP: Nitrogen Mustard, NM, NSC-762; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213; plus Prednisone, PRED, NSC-10023.

Arm II: No Chemotherapy.

STRATIFICATION BY: Participating institutions, tumor type (medulloblastoma or ependymoma).

SPECIAL STUDY PARAMETERS: Chest x-ray, skeletal survey and/or bone scan, CAT scan, myelogram when indicated.

END POINTS: Length of survival, metastasis outside CNS, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Approximately 52 patients (26 each tumor type) to be entered to each arm; accrual estimated at about 30 patients/year.

DOSAGE SCHEDULE:

Regimen A: Surgery is performed to reduce the bulk of the tumor as much as possible and/or measure the size of the tumor. As soon as the surgical wound is healed, patients 3 years of age or younger with medulloblastoma receive a tumor dose of 4000 rads midplane and 5000 rads to the posterior fossa. Patients over 3 years of age receive 3500 rads midplane and 4500 rads to the posterior fossa. These patients simultaneously receive 2500 rads (3 years of age or younger) or 3000 rads (over 3 years of age) to the spinal subarachnoid space. Patients with ependymoma receive a tumor dose of 3500 rads plus 1500-rad boost (under 3 years of age) or 4000 rads plus 1500-rad boost (age 3 or older). Simultaneously they receive 2500 rads (under 3 years of age) or 3500 rads (3 years of age or older) to the spinal subarachnoid space. Detailed Radiotherapy target area descriptions and schedules are given in the protocol. Patients are randomized for Chemotherapy plus Hormone Therapy after a 4-week rest period.

Arm I: MOPP: NM - 6 mg/sqm on days 1 and 8, iv push; VCR - 1.4 mg/sqm on days 1 and 8, iv push thru tube of running iv; PCB - 50 mg po on day 1, then 100 mg on days 2 thru 10; PRED - 40 mg po on days 1 thru 10, tapering off on days 11 thru 13. Treatment begins 4 weeks following Radiotherapy and is repeated q 4 weeks for 12 courses. Complete neurologic examination at termination of study.

Arm II: No further treatment.

Dosage modifications for toxicity are given.

DOSAGE FORMS: NM - 10 mg vials; VCR - 1 and 5 mg ampules; PCB - 50 mg capsules; PRED - 5, 20 and 50 mg capsules.

DATE SUMMARIZED: 02/80

13.0018 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR RECURRENT GLIOMA

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PROTOCOL NUMBER(S) SWOG-7980

OBJECTIVES:

I. Determine the efficacy of cis-platinum in the treatment of gliomas recurrent after prior therapy with irradiation, plus or minus chemotherapy.

II. Determine the duration of response and survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients at least 15 years of age with gliomas (Grade I-IV) that have recurred following cranial irradiation, with no prior exposure to DDP, and with evaluable lesions on either CT or radionuclide brain scan. Patients must have been off all previous chemotherapy or radiotherapy for the 4 weeks prior to entry, have recovered from toxic effects of that therapy, and have adequate hematologic, renal, and liver function. (This protocol replaces SWOG-7812, which was closed to adults in February, 1980.)

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875. Patients who are symptomatic neurologically are given glycerol or dexamethasone.

STRATIFICATION BY: Participating institutions, disease stage.

SPECIAL STUDY PARAMETERS: CT or radionuclide brain scan, serum creatinine and BUN.

END POINTS: Objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Accrual of 50 patients will be required; additional accrual will be decided by review.

DOSAGE SCHEDULE:

After adequate hydration, CACP - 35 mg/sqm iv for 3 consecutive days in each of 3 weeks. Second and third courses can be initiated in 3-4 weeks if blood counts have recovered and serum creatinine is less than 1.5 mg percent (males) and 1.2 mg percent (females), the BUN is equal to or less than 25 mg percent, and the creatinine clearance is equal to or greater than 60 cc/minute. Patients on glycerol or dexamethasone must wait 48 hours before initiating CACP treatment. A minimum of two courses is required.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 05/80

13.0019 PHASE III RADIOTHERAPY WITH/WITHOUT CCNU CHEMOTHERAPY FOR INCOMPLETELY RESECTED BRAIN GLIOMAS GRADE I AND II

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7983

OBJECTIVES:

I. Compare the survival of patients with incompletely resected Grade I and II gliomas treated with radiation alone versus radiation plus CCNU. This is the major objective of this study.

II. Compare the effectiveness of radiation therapy versus radiation therapy plus CCNU for remission induction and duration of remission. Because many of these patients will have poorly or non-measurable disease, this objective will be only secondary.

PROTOCOL ENTRY CRITERIA: Patients at least 15 years of age with histologically confirmed, incompletely resected primary Grade I and II astrocytoma, with surgery and diagnosis within the preceding 6 weeks, with no previous malignancy (except adequately treated skin cancer) and with no prior chemotherapy (corticosteroid therapy is acceptable) or primary tumor radiotherapy to the brain or overlying structures. Patients with cystic cerebellar astrocytoma are not eligible.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy plus Single-agent Chemotherapy. Cobalt-60 or 2-6 MeV x-ray; plus CCNU, NSC-79037.

Arm II: Radiotherapy. Cobalt-60 or 2-6 MeV x-ray. In event of relapse, CCNU.

STRATIFICATION BY: Participating institutions, tumor grade (astrocytoma Grade I or II), degree of resection (biopsy only vs. partial resection), performance status (0-1 vs. greater than 1).

SPECIAL STUDY PARAMETERS: CAT scan or isotope brain scan. Lumbar puncture and cerebrospinal fluid examination, electroencephalogram, arteriogram, ventriculogram, myelogram and echogram are performed as individually indicated. For posterior fossa lesions, cytological examination of the CSF is suggested.

END POINTS: Response/remission rate, objective tumor response, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Total of 80 patients, 40/arm, will be entered and followed for life.

DOSAGE SCHEDULE:

Arm I: Co-60 or 2-6 Mev x-rays - 5,500 rads in 32 fractions 5 days/week (24 hours between doses) for 6.5-7 weeks. CCNU - 100 mg/sqm po, initial dose 2 days prior to Radiotherapy, repeated at 6-week intervals. Dosage modifications according to nadirs of WBC and platelets. If complete or partial response, or stabilization of disease occurs, CCNU will be continued for not longer than total of 2 years, or until relapse. Cerebral edema controlled by dexamethasone - 10 mg/sqm parenterally or po daily in divided doses during first 2-4 weeks of Radiotherapy, tapered over next 2 weeks, then discontinued.

Arm II: Co-60 or 2-6 MeV x-rays - 5,500 rads in 32 fractions 5 days/week (24 hours between doses) for 6.5-7 weeks. Dexamethasone as in Arm I. If relapse occurs, CCNU - 100 mg/sqm q 6 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CCNU - 10, 40 and 100 mg capsules.

DATE SUMMARIZED: 05/80

13.0020 A MASTER PROTOCOL: DMSO TO ENABLE STANDARD CHEMOTHERAPEUTIC DRUGS (ADR OR CTX) TO PASS THE BLOOD-BRAIN BARRIER IN TREATMENT OF BRAIN TUMORS

Kaplan, R. S., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-8013

OBJECTIVES:

I. Determine whether dimethylsulfoxide (DMSO) can promote the achievement of therapeutic levels in brain tumors, brain and CSF of systemically administered anti-cancer drugs that do not normally cross the blood–brain barrier.

II. Determine whether certain antineoplastic agents (initially, cyclophosphamide and adriamycin, Addenda A and B, August 1980) that have wide ranges of efficacy in tumors outside the CNS can also be effective against brain tumors when administered with DMSO.

PROTOCOL ENTRY CRITERIA: Patients 60 years of age or younger with histologic, biopsy-documented malignant primary or metastatic brain tumors. The disease must be progressive as indicated by CAT scan after primary treatment with radiotherapy with or without surgery, and must be measurable. Patients must not be cachectic, previously bedridden, or preterminal and must be capable of adequate oral intake. Renal and hepatic function must be normal (creatinine less than 1.4 mg percent and normal SGOT, SGPT, and bilirubin). The patient's corticosteroid therapy dosage requirement must be known and stable or increasing at the time of initiating therapy.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Dimethylsulfoxide, DMSO, NSC-763; Adriamycin, ADR, NSC-123127, or Cyclophosphamide, CTX, NSC-26271.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Isotope brain scan, CAT brain scan, radiographic and/or nuclide assessment of extra-CNS tumor if present, Coombs test, serum haptoglobin, EKG, ophthalmologic evaluation.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 14-20 patients will be entered.

DOSAGE SCHEDULE:

DMSO - 1 g/kg iv over 90 minutes; ADR - 60 mg/sqm iv over 5-10 minutes midway during DMSO infusion; or CTX - 1,500 mg/sqm (patients with no previous nitrosoureas) or 1,250 mg/sqm (patients with previous nitrosoureas), iv over 1 hour beginning 15-30 minutes after DMSO infusion is begun. Repeat q 3 weeks. A minimum of 2 courses (6-8 weeks of therapy) is required for evaluation. Remove from study patients with progressive tumor. Stable or responding patients continue therapy until progression or cumulative toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

13.0021 PHASE I-II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE FOR RECURRENT PRIMARY OR METASTATIC BRAIN TUMORS

Kaplan, R. S., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-8029

OBJECTIVES:

I. Determine whether aziridinylbenzoquinone (AZQ) has antitumor activity against primary or metastatic brain tumors and, if so, establish an approximate rate of response and duration of response.

II. Determine the toxicities and maximally tolerated dose of AZQ in patients with brain tumors.

PROTOCOL ENTRY CRITERIA: Patients with malignant primary brain tumors: glioblastoma, multiforme, malignant astrocytoma (Grades III or IV), medulloblastoma; or recurrent low-grade glial tumors: benign astrocytoma (Grades I or II), oligodendroglioma, ependymoma, gliomas (brain stem, cerebellar, or optic nerve); or histologic diagnosis of brain metastasis including refractory meningeal metastatic tumors. All patients must have a brain tumor measurable by CAT scan and progressing disease after primary treatment with radiation therapy with or without surgery. Patients must be less than 70 years of age; there must be adequate hematologic function and normal renal and hepatic function. Previously bedridden and preterminal patients are not eligible. Patients must be capable of adequate oral intake. All prior therapy must have been completed at least 6 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Aziridinylbenzoquinone, AZQ, NSC-182986.

STRATIFICATION BY: Primary brain tumors vs. brain metastases.

SPECIAL STUDY PARAMETERS: Neurologic examination, measurement of extra-CNS tumors, isotope brain scan, CT brain scan, CBC, platelet count, differential, serum chemistries.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Initially 28 patients will be entered.

DOSAGE SCHEDULE:

AZQ - 17.5 mg/sqm as a freely running iv infusion over 30 minutes on days 1 and 8. Repeat course q 28 days, or delay until the patient has recovered from drug-induced toxicity. All patients should receive at least 2 courses. Stable or responding patients continue treatment until disease progression or unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZQ - 10 mg vials.

DATE SUMMARIZED: 12/80

13.0022 CHEMOTHERAPY WITH DAG/TZT/VP-16 OR PCB/VCR/CCNU FOR PRIMARY INTRACRANIAL NEOPLASMS

Edmondson, J. H., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-767202

OBJECTIVES:

I. Compare the effectiveness, safety and morbidity of 2 chemotherapeutic regimens, galactitol plus Baker's antifol plus VP-16 or procarbazine plus vincristine plus CCNU, in the treatment of recurrent and disseminated primary neoplasms of the neuroaxis in patients eligible for concomitant radiation therapy or in patients who have received maximal radiation therapy.

II. Determine acceptable and effective dosages, schedules and toxicity of agents used.

III. Ascertain the immunologic status of patients with seeding neoplasms of the CNS prior to, during and following therapies as well as at the time of recurrence.

IV. Ascertain the frequency of detectable neoplastic cells in the cerebrospinal fluid and correlate this with evidence of clinical recurrence, immunologic status, effectiveness of therapy, and establish the significance of detectable neoplastic cells in the CSF in the absence of overt seeding.

V. Evaluate the effectiveness of a single chemotherapeutic regimen in the treatment of recurrent intrinsic brain stem gliomas in a pilot fashion.

VI. Establish precedent, methodology and controls for future reference which possibly will lead to more effective therapeutic modalities.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed seeding primary CNS neoplasms who have received accepted radiation therapy and present with demonstrated recurrence, or with gross evidence of dissemination.

Patients with posterior 3rd ventricular neoplasms in whom there is cytological and/or other evidence of dissemination through the neuroaxis, and clinically diagnosed intrinsic lesions of the brain stem who have received accepted radiation therapy and present with evidence of recurrence.

PROTOCOL OUTLINE: Randomized study. Randomize patients with primary CNS neoplasms with propensity to seed through the neuroaxis to Arm I or Arm II. Enter patients with intrinsic brain stem glioma to Arm I.

Arm I: 3-Drug Combination Chemotherapy. Dianhydrogalactitol, Galactitol, DAG, NSC-132313; Baker's antifol, TZT, NSC-139105; VP-16, NSC-141540.

Arm II: 3-Drug Combination Chemotherapy. Procarbazine, PCB, NSC-77213; Vincristine, VCR, NSC-67574; CCNU, NSC-79037.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Immunologic studies - lymphocyte blastogenesis, T and B cell, monocyte chemotaxis; EMI scan.

END POINTS: Response/remission rate, objective tumor response, duration and quality of response, survival time, toxicity/morbidity of treatment, recurrence rate.

CURRENT STATUS: About 15 patients per year will be entered.

DOSAGE SCHEDULE:

Arm I: DAG - 15 mg/sqm, iv, for days 1 through 5; TZT - 125 mg/sqm, iv, for days 1 through 3; VP-16 - 75 mg/sqm, iv, on days 1, 3 and 5.

Arm II: PCB - 100 mg/sqm, po, for days 1 through 14; VCR - 1.4 mg/sqm, iv, on days 1 and 8; CCNU - 75 mg/sqm, po, on day 1.

Repeat therapy of both Arms q 5 weeks for the 1st year and q 10 weeks during the 2nd year, and then discontinue or until treatment failure. Carry out radiation therapy in all situations in which it is felt such will benefit the patient.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DAG - 50 mg vials; TZT - 100 and 250 mg vials; VP-16 - 100 mg ampules; VCR - 1 and 5.1 mg vials; PCB - 50 mg capsules; CCNU -20, 40 and 100 mg capsules.

DATE SUMMARIZED: 04/77

PATIENT ACCRUAL: 00090179

13.0023 COMBINATION CHEMOTHERAPY WITH O-DAP (VCR/DAG/ADR/CACP), DV (DAG/VP-16) OR BT (BCNU/TZT) FOR RECURRENT CNS TUMORS

Eagan, R. T., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-787201

OBJECTIVES:

I. Evaluate the combination of O-DAP: vincristine (VCR)/dianhydrogalactitol (DAG)/adriamycin (ADR)/cis-platinum (CACP) as induction treatment irradiation.

II. Evaluate the combination of DV: DAG/VP-16 as maintenance therapy for patients in response after 6 courses of O-DAP.

III. Evaluate the combination of BT: BCNU/Baker's antifol (TZT) in patients failing the above chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with supratentorial and/or nonseeding brain tumor confirmed histologically or by CAT scan. Patients must have disease progression after radiotherapy and the tumor must be visible by CAT scan or radionucleotide brain scans. Patients must have adequate bone marrow, hepatic, renal and cardiac function.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients without prior Chemotherapy or prior BCNU to Regimen A, followed by Regimen B, patients with prior VP-16 to Regimen A followed by Regimen C. Enter patients with prior therapy with DAG with or without VP-16 or with cardiac or renal disease to Regimen C.

Regimen A: 4-Drug Combination Chemotherapy plus Hormone Therapy. O-DAP: Vincristine, VCR, NSC-67574; Dianhydrogalactitol, DAG, NSC-132313; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875; Prednisolone, PRDL, NSC-9900.

Regimen B: 2-Drug Combination Chemotherapy. DV: DAG; VP-16, NSC-141540.

Regimen C: 2-Drug combination Chemotherapy. BT: BCNU; NSC-409962; Baker's Antifol, TZT, NSC-139105.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: CAT scan with contrast.

END POINTS: Response/remission rate, disease-free interval or previous treatment with BCNU or VP-16.

CURRENT STATUS: At least 42 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: O-DAP: DAG - 35 mg/sqm iv infusion at 0 and 5 hours, with mannitol infusion beginning at hour 1; ADR - 40 mg/sqm iv at hour 3; CACP - 40 mg/sqm iv directly after ADR; VCR - 1.2 mg/sqm iv directly after CACP; PRDL - 125 mg/sqm iv directly after VCR. Repeat course q 4 weeks for 6 courses except for patients with prior VP-16 therapy who continue on O-DAP until disease progression and then enter Regimen C. All other patients enter Regimen B.

Regimen B: DV: Enter cohorts of 3 patients each to DAG - 35 (40 and 45) mg/sqm iv at hours 0 and 5 until tolerable dosage level is established; VP-16 - 200 mg/sqm (escalating to 250 in next 3 patients if tolerated) beginning at hour 1 after DAG infusion. Repeat course q 5 weeks, until disease progression. Then enter patients without previous therapy to Regimen C; remove patients with prior BCNU therapy from study.

Regimen C: BT: Enter cohorts of 3 patients each to BCNU - 40 (45, 50 and 55) mg/sqm iv push followed by TZT - 175 (200, 225) mg/sqm iv infusions on days 1, 2 and 3. Treat 3 patients at each dosage level until tolerance is established. Repeat course q 6 weeks until disease progression, then remove patients from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DAG - 50 mg vials; ADR - 10 and 50 mg vials; CACP -10 mg vials; VCR - 1 and 5 mg vials; VP-16 - 100 mg ampules; BCNU - 100 mg vials; TZT - 100 and 250 mg vials.

DATE SUMMARIZED: 12/78

PATIENT ACCRUAL: 00090279

13.0024 PHASE II COMBINATION CHEMOTHERAPY WITH DIANHYDROGALACTITOL/BCNU FOR PRIMARY INTERCRANIAL BRAIN TUMORS

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PROTOCOL NUMBER(S) MAYO-797201

OBJECTIVES:

I. Evaluate the combination of dianhydrogalactitol/BCNU in patients with primary intracranial neoplasms.

II. Assess the long term (chronic) toxicity of the drug combination.

PROTOCOL ENTRY CRITERIA: Patients with primary intracranial tumor, confirmed by CT scan, that persists after 8 weeks of initial therapy and produces some neurological signs or symptoms. Patients must have adequate hematologic and renal function and no prior therapy with DAG or a nitrosourea.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. BCNU, NSC-409962; Dianhydrogalactitol, DAG, NSC-132313.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: CT brain scan.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 5 to 20 patients will be entered.

DOSAGE SCHEDULE:

BCNU - 90 mg/sqm iv infusion on day 1. DAG - 70 mg/sqm iv infusion on day 1. Repeat course q 5 weeks for 3 cycles, then re-evaluate patients. Remove from study patients with progressive disease, continue patients with complete response for 4 additional courses given q 5 to 6 weeks. Continue patients with stable or partial response on therapy given q 5 to 6 weeks until complete response or disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

13.0025 PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE FOR RECURRENT PRIMARY BRAIN TUMORS

Eagan, R. T., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America

PROTOCOL NUMBER(S) MAYO-807202

OBJECTIVES:

I. Conduct a Phase II study of aziridinylbenzoquinone in patients with primary brain tumors recurrent after prior irradiation.

PROTOCOL ENTRY CRITERIA: Patients with primary intracranial neoplasm, diagnosed by biopsy or CT scan/angiogram, progressive after prior cerebral irradiation. Tumor must be visible on CT scan of brain. Patients must have adequate hematologic, renal, and hepatic function. Chemotherapy with nitrosoureas alone within the 6 weeks prior to entry is not allowed and patients must not receive chemotherapy with a nitrosourea in combination within 4 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Aziridinylbenzoquinone, AZQ, NSC-182986.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; CT brain scan with contrast; neurological examination.

END POINTS: Response/remission rate, objective tumor response, subjective assessment.

CURRENT STATUS: 30 patients with prior chemotherapy and 20 patients without prior chemotherapy will be entered.

DOSAGE SCHEDULE:

AZQ - 22.5 mg/sqm iv over 5-15 minutes on day 1 q 4 weeks for patients with prior chemotherapy. Patients with no prior chemotherapy receive AZQ - 27.5 mg/sqm iv over 5-15 minutes on the same schedule. Retreatment interval may be prolonged up to 6 weeks on the basis of hematologic and other clinical parameters. Patients continue treatment until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZQ - 10 mg vials.

DATE SUMMARIZED: 11/80

13.0026 CHEMOTHERAPY WITH INTRA-ARTERIAL CIS-PLATINUM FOR UNRESECTABLE INTRACEREBRAL NEOPLASMS

Stewart, D. J., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-273; MDA-DT-7821

OBJECTIVES:

I. Determine the therapeutic efficacy and toxicity of cis-platinum (CACP) injected into the carotid artery for patients with unresectable intracerebral malignancies.

PROTOCOL ENTRY CRITERIA: Patients with symptomatic, recurrent unresectable intracerebral malignant tumors. Patients must have adequate hematologic and renal status and have had no therapy for the preceding 4 weeks.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: At least 20 patients will be entered.

DOSAGE SCHEDULE:

Enter cohorts of 3 patients each to CACP - 60, 90 and 120 mg/sqm intra-arterial (carotid artery). Repeat course q 4 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

13.0027 CIS-PLATINUM CHEMOTHERAPY PLUS RADIOTHERAPY FOR RESECTED, RESIDUAL OR RECURRENT BRAIN TUMOR

Stewart, D. J., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-302; MDA-DT-7850

OBJECTIVES:

I. Determine the efficacy of cis-platinum (CACP) administered on a weekly schedule along with cranial irradiation in the treatment of malignant primary brain tumors.

II. Determine qualitative and quantitative toxicity of CACP administered in this fashion.

III. Determine duration of response and duration of survival of patients receiving this therapy.

PROTOCOL ENTRY CRITERIA: Patients over 15 years old with histologically proven resected, residual or recurrent glioma. Patients must have adequate bone marrow, liver and renal function and must not have had prior cranial radiotherapy or chemotherapy with CACP. (Patients who have received prior cranial irradiation will receive CACP alone, without irradiation. Revision, January 1979.) They must have been off any prior chemotherapy for at least 4 weeks and must have recovered from any toxic effects. (Creatinine clearance must be greater than 60 cc/min. Revision, January 1979.)

PROTOCOL OUTLINE: Nonrandomized study. Compare patients entered to this study to patients receiving Radiotherapy alone.

Radiotherapy plus Single-agent Chemotherapy. Megavoltage radiation, plus cis-Platinum, CACP, NSC-119875. (Chemotherapy alone in patients with prior cranial irradiation, Revision January 1979.)

STRATIFICATION BY: Complete disease resection vs. partial resection vs. recurrent disease.

SPECIAL STUDY PARAMETERS: Brain scan.

END POINTS: Response/remission rate, recurrence rate, survival time.

CURRENT STATUS: At least 14 evaluable patients in each stratification (completely resected, partially resected, recurrent) will be entered.

DOSAGE SCHEDULE:

For patients without prior cranial irradiation: Radiotherapy - 6000 rad given in 7 weeks (5 fractions/week) to the cranium; CACP - 40 mg/sqm iv q 7 days during period of radiotherapy (less than 24 hours before fractions 1, 6, 11, 16, 21, 26, and 31 of cranial irradiation. Revision, January 1979.) Rest 3 to 4 weeks, then resume CACP therapy - 120 mg/sqm given once q 3 to 4 weeks.

For patients with prior cranial irradiation: As per revision, January 1979, CACP - 120 mg/sqm once q 3 to 4 weeks. No additional Radiotherapy.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 04/80

13.0028 PHASE II CHEMOTHERAPY WITH AZIRIDINYLBENZOQUINONE FOR MALIGNANT PRIMARY BRAIN TUMOR

Feun, L. G., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-420; MDA-DT-8048

OBJECTIVES:

I. Determine the efficacy and toxicity of aziridinylbenzoquinone in the treatment of malignant primary brain tumors.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with histologically proven Grade I-IV astrocytoma or patients presumed to have this malignancy on the basis of clinical evaluation. Patients must have intracranial lesions evaluable by CT scan. There must be adequate bone marrow, liver, and renal function unless this therapy is indicated as a life-saving measure. Patients must have been off all previous chemotherapy and radiotherapy for the 3 weeks prior to entry. Patients with prior chemotherapy and/or cranial irradiation must show evidence of tumor recurrence or progression.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Aziridinylbenzoquinone, AZQ, NSC-182986.

STRATIFICATION BY: Recurrent tumor grade: I-II vs. III-IV.

SPECIAL STUDY PARAMETERS: CBC, platelet count and differential, SMA, urinalysis, neurological examination, tumor measurements, CT scan of brain.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 25 patients will be entered.

DOSAGE SCHEDULE:

AZQ - 8 mg/sqm iv over 1 hour for 5 days q 4 weeks for good-risk patients (adequate bone marrow reserve, no prior treatment with Mitomycin-C or nitrosoureas). Poor-risk patients (inadequate bone marrow reserve, prior treatment with Mitomycin-C or nitrosoureas) receive a reduced dose, AZQ - 6 mg/sqm, on the same schedule. A minimum of 2 courses is required for an adequate trial. Patients continue therapy for 2 years or for 1 year after achieving complete remission, whichever is shorter. Patients with progressive disease or unacceptable stable disease after an adequate trial go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AZQ - 10 mg vials.

DATE SUMMARIZED: 11/80

13.0029 COMBINATION CHEMOTHERAPY WITH BCNU/IMIDAZOLE MUSTARD/PCB/VM-26/PRED FOR REFRACTORY PRIMARY BRAIN TUMORS

Samuels, M. L., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-82

OBJECTIVES:

I. Study the rate of response of brain tumors to this chemotherapy regimen.

II. Determine the length of remission under Maintenance.

III. Determine the toxicity, mainly hematological, of the regimen.

PROTOCOL ENTRY CRITERIA: Patients with proven primary brain tumor who have had biopsy with maximum resection followed by radiotherapy and who have shown subsequent neurologic deterioration and increased requirement for steroids and/or objective tumor regrowth through DAT scan, EEG and/or radionuclear brain scan. Include the following histologic diagnosis - astrocytoma, grade II, III, and IV (glioblastoma multiforme), polar spongioblastoma, mixed glioblastoma and fibrosarcoma, oligodendroglioblastoma, primary reticulum cell sarcoma of the brain, medulloblastoma and ependymoma.

PROTOCOL OUTLINE: Nonrandomized study. All patients enter Regimen A. Patients with unequivocal recurrence are concurrently treated on Regimen B.

Regimen A: 2-Drug Combination Chemotherapy. BCNU, NSC-409962; Imidazole Mustard, TIC, NSC-82196.

Regimen B: 2-Drug Combination Chemotherapy plus Hormone Therapy. Procarbazine, PCB, NSC-77213; VM-26, NSC-122819; Prednisone, PRED, NSC-10023.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Radionuclide, DAT scans.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 14 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: BCNU - 100 mg/sqm in 100 cc D5W on day 4; TIC - 300 mg/sqm in 100 cc D5W rapid infusion on days 1, 2, 3, 4, and 5. Repeat course q 6 weeks, but begin 2nd course on day 35 if no myelosuppression is noted at this point. A phenothiazine or other emetic should be given prior to each injection of TIC and BCNU.

Regimen B: PCB - 50 mg po on day 1, 100 mg po on day 2, 200 mg po on day 3, 150 mg/sqm po on days 4 to 14; VM-26 - 130 mg/sqm in 100 cc D5W infused over 45 minutes on days 1, 8, and 14. PRED - 40 mg/po on day 1 to day 14. Repeat course q 29 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 09/77

13.0030 PHASE I-II CHEMOTHERAPY WITH BCNU PLUS AUTOLOGOUS BONE MARROW REINFUSION FOR RECURRENT PRIMARY BRAIN TUMORS

Parker, L., (617-247-6075) Sidney Farber Cancer Center Inc., 44 Binney St., Boston, Massachusetts, 02115, United States of America

PROTOCOL NUMBER(S) SFCC-79012

OBJECTIVES:

I. Determine the effects of high dose BCNU plus autologous bone marrow reinfusion for recurrent, intracranial (intracerebral and meningeal) malignancy of primary origin.

II. Determine organ specific toxicity.

III. Evaluate the effect of autologous bone marrow reinfusion on BCNU myelosuppression.

IV. Assess correlation between CT scan evidence and clinical response.

PROTOCOL ENTRY CRITERIA: Patients 18 to 60 years of age with histologically confirmed recurrence, following surgery or radiotherapy, of intracerebral and meningeal malignancy of primary origin. Patients must have a Karnofsky performance status of at least 60 and must not have prior chemotherapy with nitrosoureas or similar stem cell poison drugs.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Immunotherapy. BCNU, NSC-409962; plus autologous reinfusion of bone marrow.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Peripheral blood colony formation unit determination (CFU-C); CT scan of brain; bone marrow aspirate and biopsy.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival, extent of tissue necrosis at autopsy.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

BCNU - 400 mg/sqm iv in 2 divided doses over 12 hours. Escalate in increments of 200 mg/sqm for cohorts of 2 to 3 patients until dose-limiting toxicity is reached; harvest bulk bone marrow aspirate immediately prior to BCNU, store at 4 degrees C, and reinfuse 48 hours after harvesting or 36 hours after BCNU administration.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

13.0031 PHASE II COMBINATION CHEMOTHERAPY WITH 5-FU/HU/6-MP/BCNU FOR RECURRENT MALIGNANT BRAIN TUMORS

Levin, V. A., (415-666-3878) University of California, Brain Tumor Research Center, 783 HSW, San Francisco, California, 94143, United States of America
PROTOCOL NUMBER(S) BTRC-7822A

OBJECTIVES:

I. Determine the efficacy of chemotherapy with 5-fluorouracil (5-FU), hydroxyurea (HU), 6-mercaptopurine (6-MP), and BCNU for patients with malignant brain tumors.

II. Evaluate the time to progression, response rates, and duration of response, as well as the quality and duration of survival.

III. Compare the results of this therapy with the previous BTRC study of BCNU/5-FU.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed primary recurrent or metastatic brain tumor where there is no clinical or radiographic evidence that supports any other diagnosis. Radiotherapy and chemotherapy must not have been administered for at least three months and six weeks, respectively, prior to entry; surgery (other than biopsy) must not have been performed for at least two months. The life expectancy must be at least six weeks. The WBC count must be 4000/cumm or greater and the platelet count 125, 000/cumm or greater. Hepatic and renal function must be adequate. Patients who have previously failed a nitrosourea schedule are treated in protocol BTRC-7822B.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. BCNU, NSC-409962; 5-Fluorouracil, 5-FU, NSC-19893; Hydroxyurea, HU, NSC-32065; 6-Mercaptopurine, 6-MP, NSC-755.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Radionuclide brain scan, CAT brain scan, clinical neurological exam, myelogram, angiogram, ventriculogram.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: Protocol remains open for non-glioblastoma malignant glioma patients as of November, 1980; 30 evaluable patients are required to complete study.

DOSAGE SCHEDULE:

BCNU - 180 mg/sqm iv over 30-45 minutes on day 1; 5-FU - 1 g/sqm/day iv continuous infusion on days 15 through 17; HU - 1600 mg/sqm po in 4 divided doses daily (on an empty stomach) on days 24 through 26; 6-MP - 400 mg/sqm po in 4 divided doses daily (on an empty stomach) on days 33 through 35. Evaluate patients on day 49 for additional courses of therapy. Repeat courses q 7 weeks until progression. Patients are followed for 2 years or until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; 5-FU - 500 mg ampules; 6-MP - 50 mg tablets; HU - 500 mg capsules.

DATE SUMMARIZED: 10/80

13.0032 PHASE II COMBINATION CHEMOTHERAPY WITH 5-FU/HU/6-MP/PCB FOR RECURRENT MALIGNANT BRAIN TUMORS

Levin, V. A., (415-666-3878) University of California, Brain Tumor Research Center, 783 HSW, San Francisco, California, 94143, United States of America
PROTOCOL NUMBER(S) BTRC-7822B

OBJECTIVES:

I. Determine the efficacy of chemotherapy with 5-fluorouracil (5-FU), hydroxyurea (HU), 6-mercaptopurine (6-MP), and procarbazine (PCB) for patients with malignant brain tumors who have failed previous nitrosourea therapy.

II. Evaluate the time to progression, response rate, and duration of response, as well as the quality and duration of survival.

III. Compare the results of this therapy with the previous BTRC study of BCNU/5-FU.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed primary recurrent or metastatic brain tumor, who have failed previous nitrosourea therapy; there must be no clinical or radiographic evidence that supports any other diagnosis. Radiotherapy and chemotherapy must not have been administered for at least three months and six weeks, respectively, prior to entry; surgery (other than biopsy) must not have been performed for at least two months. The life expectancy must be six weeks or longer. The WBC count must be 4000/cumm or greater and the platelet count 125, 000/cumm or greater. Hepatic and renal function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. Procarbazine, PCB, NSC-77213; 5-Fluorouracil, 5-FU, NSC-19893; Hydroxyurea, HU, NSC-32065; 6-Mercaptopurine, 6-MP, NSC-755.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Radionuclide brain scan, CAT brain scan, clinical neurological exam, myelogram, angiogram, ventriculogram.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: Protocol remains open for non-glioblastoma malignant glioma patients as of November, 1980; 30 evaluable patients are required to complete study.

DOSAGE SCHEDULE:

PCB - 150 mg/sqm po daily for 14 days; 5-FU - 1 g/sqm/day iv continuous infusion on days 21 through 23; HU - 1600 mg/sqm po in 4 divided doses daily (on an empty stomach) on days 30 through 32; 6-MP - 400 mg/sqm po in 4 divided doses (on an empty stomach) on days 39 through 41. Evaluate patients on day 55 for additional courses of therapy. Repeat courses q 8 weeks until progression, at which time other therapy may be given at the discretion of investigator. Patients will be followed until death.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PCB - 50 mg capsules; 5-FU - 500 mg ampules; HU - 500 mg capsules; 6-MP - 50 mg tablets.

DATE SUMMARIZED: 10/80

13.0033 PHASE II PILOT CHEMOTHERAPY WITH PROCARBAZINE AND HYDROXYUREA PRIOR TO AND DURING IRRADIATION FOR MEDULLOBLASTOMA

Levin, V. A., (415-666-3878) University of California, Brain Tumor Research Center, 783 HSW, San Francisco, California, 94143, United States of America
PROTOCOL NUMBER(S) BTRC-7922

OBJECTIVES:

I. Determine whether the addition of chemotherapy, following surgery and prior to and during radiotherapy, in children with medulloblastoma will: decrease the incidence of local recurrence; decrease the incidence of metastases; increase the time to recurrence; and increase the survival rate.

II. Document the toxicity caused by the combined treatment.

PROTOCOL ENTRY CRITERIA: Patients with a medulloblastoma, neuroblastoma or ependymoblastoma confirmed by histopathological or clinical and radiographic evidence that supports no other diagnosis. There must be no prior radiotherapy or myelotoxic chemotherapy. Hepatic and renal function must be adequate

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy plus Radiotherapy. Procarbazine, PCB, NSC-77213; Hydroxyurea, HU, NSC-32065; plus megavoltage irradiation of the whole brain and spinal cord with Co-60 or photons to 8 MeV.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Full myelogram before radiotherapy to determine spinal cord dose and/or boost, radionuclide brain scan, CT brain scan, clinical neurological exam, lumbar puncture, angiogram, ventriculogram.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length of survival.

CURRENT STATUS: 12 patients have been treated as of November, 1980; 30 evaluable patients will be required.

DOSAGE SCHEDULE:

PCB - 100 mg/sqm po on days 1 through 14, beginning 2 weeks after surgery; HU - 1100 mg/sqm po in 4 divided doses (on an empty stomach) daily on days 15 through 58 during radiation therapy. Radiotherapy: total dose of 5500 rads to posterior fossa in fractions of 180-200 rads/day on days 15 through 58; 3500 rads to entire cranial field and 2500 rads to spinal cord field in fractions of 180-200 rads/day on days 29 through 58. For spinal metastases demonstrated in myelogram, an additional 1500 rads may be given to those areas during the last 4 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: PCB - 50 mg capsules; HU - 500 mg capsules.

DATE SUMMARIZED: 10/80

13.0034 PHASE II CHEMOTHERAPY WITH DIBROMODULCITOL (DBD) FOR RECURRENT MEDULLOBLASTOMA AND EPENDYMOMA

Levin, V. A., (415-666-3878) University of California, Brain
Tumor Research Center, 783 HSW, San Francisco, California,
94143, United States of America
PROTOCOL NUMBER(S) BTRC-8022

OBJECTIVES:

I. Evaluate the time to progression during treatment of recurrent medulloblastoma and ependymoma with dibromodulcitol.

II. Evaluate response rate, duration of response, and the quality and duration of survival.

PROTOCOL ENTRY CRITERIA: Patients with a primary recurrent medulloblastoma or ependymoma with either histologic confirmation or clinical and radiographic evidence that supports no other diagnosis; they must have failed previous chemotherapy or radiotherapy. The life expectancy must be at least 6 weeks and at least 6 weeks must have elapsed since prior chemotherapy, 3 months since radiotherapy and 2 months since surgery or biopsy. Liver and renal function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dibromodulcitol, DBD, NSC-104800.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Radionuclide brain scan, CT brain scan, clinical neurological examination, myelogram, lumbar puncture, angiogram.

END POINTS: Response/remission rate, duration of response, recurrence rate, toxicity/morbidity of treatment, objective tumor response, length and quality of survival.

CURRENT STATUS: 20 patients have been entered as of November 1980; 20 patients per tumor type will be required.

DOSAGE SCHEDULE:

DBD - 400 mg/sqm po in 4 divided doses daily for 45 days or until counts drop by 50 percent. Treatment may be resumed only after WBC count returns to at least 4000/cumm and/or platelet count to at least 125,000/cumm. If DBD treatment is interrupted because of hematological toxicity, the patient must have a 3-week rest period, even though the counts return to normal within that period. In the absence of hematological toxicity after 45 days of treatment with DBD, a 20 percent dose increase may be attempted after a 3-week rest period. DBD may be given on an out-patient basis; no food should be taken for 2 hours prior to administration of the drug.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: DBD - 100 mg capsules.

DATE SUMMARIZED: 10/80

13.0035 RADIOTHERAPY PLUS CHEMOTHERAPY WITH BCNU OR DBD OR CHEMOTHERAPY ALONE WITH VM-26 OR VP-16 FOR BRAIN TUMORS

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Treatment Group, 200 First Street, S.W., Rochester, Minnesota,
55901, United States of America
PROTOCOL NUMBER(S) NCCTG-797251; MAYO-797251

OBJECTIVES:

I. Compare radiotherapy plus BCNU vs. radiotherapy plus dibromodulcitol (DBD) in newly diagnosed patients with glioma and no prior radiotherapy or chemotherapy.

II. Compare VM-26 vs. VP-16213 (VP-16) in patients with primary non-seeding brain tumor recurrent after radiotherapy with or without any prior chemotherapy.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed supratentorial and/or non-seeding brain tumor. Patients with nonoperable tumors unable to provide histologic confirmation of disease are eligible if CT examination (a radionucleotide brain scan will suffice for patients unable to undergo CT examination) of the brain and/or angiogram plus neurological examination strongly suggest a primary brain tumor. Patients who have previous radiotherapy given alone following surgery must present evidence of disease progression. Patients with seeding neoplasm (medulloblastoma or ependymona) are not eligible. Adequate renal, hepatic, and hematologic function is required. Patients with prior chemotherapy with any of the protocol agents are ineligible for entry into the portion of the protocol using the previously administered agents.

PROTOCOL OUTLINE: Randomized study. Patients with no prior Radiotherapy or Chemotherapy, with histological evidence of astrocytoma or with Grade 3 or 4 tumors enter Regimen A. Patients with disease progression following prior Radiotherapy with or without prior Chemotherapy and those with astrocytoma of any grade enter Regimen B. Regimen A patients are randomized to Arms I and II, Regimen B patients to Arms III and IV.

Regimen A:

Arm I: Radiotherapy plus Single-agent Chemotherapy. Cerebral irradiation plus BCNU, NSC-409962.

Arm II: Radiotherapy plus Single-agent Chemotherapy. Cerebral irradiation plus Dibromodulcitol, DBD, NSC-104800.

Regimen B:

Arm III: Single-agent Chemotherapy. VM-26, NSC-122819.

Arm IV: Single-agent Chemotherapy. Vp-16213, VP-16, NSC-141540.

STRATIFICATION BY: Regimen A: age (less vs. more than 55); extent of surgery (none vs. biopsy vs. subtotal or total resection); tumor grade (unknown vs. 3 vs. 4). Regimen B: prior chemotherapy (yes vs. no); time to recurrence from start of CNS radiotherapy (less than vs. equal to or more than 6 months); tumor grade (unknown vs. 1 to 2 vs. 3 to 4).

SPECIAL STUDY PARAMETERS: Neurological exam, CAT scan with contrast.

END POINTS: Toxicity/morbidity of treatment, disease-free interval, objective tumor response, length of survival.

CURRENT STATUS: 300 patients will be entered in 2 years.

DOSAGE SCHEDULE:

Regimen A: Chemotherapy and Radiotherapy should be started on the same day, within 14 days of Surgery or diagnosis.

Arm I: Radiotherapy. 4500-4600 rads in 5 fractions/week at 900-1000 rads/week to whole brain plus an additional boost to tumor of 1000-1500 rads delivered at same dose rate as to brain; BCNU - 200 mg/sqm iv in a 1-hour infusion on day 1. Repeat at 7-week intervals.

Arm II: Radiotherapy as in Arm I. DBD - 200 mg/sqm po on days 1 through 10, given at bedtime. Repeat at 5-week intervals.

Regimen B:

Arm III: VM-26 - 30 mg/sqm iv 30-minute infusion on days 1 through 5. Repeat at 4-week intervals.

Arm IV: VP-16 - 60 mg/sqm iv 30-minute infusion on days 1 through 5. Repeat at 4-week intervals.

Patients who show progression in Regimen A may be entered to Regimen B. Patients are treated in Regimen B until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; DBD - 50 mg tablets; VM-26 - 50 mg vials; VP-16 - 100 mg ampules.

DATE SUMMARIZED: 09/80

BRAIN AND OTHER CNS TUMORS

13.0036 RADIOTHERAPY WITH OR WITHOUT ADJUVANT IMMUNOTHERAPY WITH LEV FOR GLIOBLASTOMA

Fischer, S. P., (215-427-7000) Episcopal Hospital, Front Street and Lehigh Ave., Philadelphia, Pennsylvania, 19125, United States of America

PROTOCOL NUMBER(S) PA-BN-1; JRD-12564/8857

OBJECTIVES:

I. Determine whether addition of levamisole (LEV) to standard therapy can prolong remission and increase survival rate.

II. Compare (for inoperable tumors) the growth rates of residual tumorsas well as survival rates in the two therapy groups.

PROTOCOL ENTRY CRITERIA: Patients with previously untreated, histologically proven glioblastoma.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Brain irradiation.

Arm II: Radiotherapy plus Immunotherapy. Brain irradiation plus Levamisole, LEV, NSC-177023.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Duration of remission; duration of survival.

CURRENT STATUS: 24 patients accrued as of February 1980.

DOSAGE SCHEDULE:

Arm I: Radiotherapy - supervoltage irradiation, 1000 rads/week for 6 weeks, to a total of 4000 rads to the entire brain followed by a boost of 2000 rads to the tumor.

Arm II: Radiotherapy as in Arm I plus concomitant (starting during the second week of Radiotherapy) LEV - 7.5 mg/kg/day po in 3 divided doses for 3 consecutive days every other week until evidence of progressing disease, up to 3 years.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 03/80

PATIENT ACCRUAL: 00240280

13.0037 PREOPERATIVE CHEMOTHERAPY WITH BCNU PLUS STANDARD OR SUPERFRACTIONATED RADIOTHERAPY FOR GLIOBLASTOMA

Pater, J. L., (613-544-9580) National Cancer Institute of Canada, Clinical Trials Group, 12 O'Kill Street, Kingston, Ontario, K7L 5E2, Canada

PROTOCOL NUMBER(S) CAN-NCIC-CE1

OBJECTIVES:

I. Study the effects of preoperative BCNU and superfractionated radiotherapy on the survival of patients with glioblastoma multiforme or malignant astrocytoma (study is designed to evaluate these two treatments independently).

PROTOCOL ENTRY CRITERIA: Patients with clinical and radiological evidence of glioblastoma multiforme or malignant astrocytoma. Patients must be between the ages of 16 and 80 years. There must be adequate bone marrow, renal, and hepatic functions. Patients must have no unrelated major medical or psychiatric illness.

PROTOCOL OUTLINE: Patients are randomized to Arms I and II for preoperative Chemotherapy; they are simultaneously randomized to Arms III and IV for postoperative Radiotherapy. All patients undergo Surgery.

Arm I: Single-agent Chemotherapy. BCNU, NSC-409962; plus steroids.

Arm II: No preoperative Chemotherapy. Steroids only.

Regimen A: Surgery. Maximal safe resection.

Arm III: Radiotherapy. Conventional fractionation dose.

Arm IV: Radiotherapy. Superfractionation dose.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic, renal, and hepatic function tests; CT scan; brain scan; detailed neurological exam; angiography; chest x-ray.

END POINTS: Duration of stable state, length of survival, quality of life.

CURRENT STATUS: 300 evaluable patients will be sought.

DOSAGE SCHEDULE:

Arm I: Chemotherapy is given 8 to 12 days prior to Surgery. BCNU - 200 mg/sqm in a single iv infusion. Appropriate neurosurgical doses of corticosteroids are given.

Arm II: Patients receive appropriate neurosurgical doses of corticosteroids only.

Regimen A: Maximal safe resection with or without an internal decompression.

Arm III: Each participating institution chooses one of four conventional radiation treatment options: 4000 rads in 20 fractions, 4600 rads in 23 fractions, 4200 rads in 21 fractions, or 4400 rads in 22 fractions. Radiotherapy should begin 1 to 2 weeks after Surgery. A boost dose of 1000 rads (in 5 fractions) is also given.

Arm IV: Each participating institution chooses one of four superfractionation radiation treatment options: 4680 rads in 60 fractions, 4914 rads in 63 fractions, 5148 rads in 66 fractions, or 5382 rads in 69 fractions. A boost of 1170 rads in 15 fractions or 1000 rads in 5 fractions may be given. Radiotherapy should begin 1 to 2 weeks after Surgery. Treatment is given over a 20-23 day period.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCNU - 100 mg bottles.

DATE SUMMARIZED: 01/81

13.0038 ADJUVANT RADIOTHERAPY AND CHEMOTHERAPY WITH MTX/VCR/PCB FOR CNS OR SPINAL TUMORS IN CHILDREN

Donoso Gonzalez, J. M., Universidad Catolica de Chile, Casilla 114-D, Santiago, Chile

PROTOCOL NUMBER(S) CHILE-SNC-178

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with intrathecal methotrexate (MTX), vincristine (VCR) and procarbazine (PCB) as adjuvant therapy to surgery and radiotherapy.

PROTOCOL ENTRY CRITERIA: Patients under 14 years of age with CNS or spinal tumors. Patients may have had either prior surgery and/or radiotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Surgery plus Radiotherapy plus 3-Drug Combination Chemotherapy. Intrathecal Methotrexate, MTX, NSC-740; Vincristine, VCR, NSC-67574; Procarbazine, PCB, NSC-77213.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Pneumoencephalogram.

END POINTS: Response/remission rate.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Surgery - curative or palliative as the tumor presents.

Radiotherapy - 3500-5500 rad in 3 to 6 weeks to the tumor, cranium and spinal column. Begin as soon as possible after surgery.

MTX - 12 mg/sqm (maximum dose 12 mg) intrathecally (it) on day 1 q 7 days for 6 months; VCR - 1.5 mg/sqm (maximum dose 2 mg) iv on day 1 q 7 days for 3 months, then q 14 days for the next 6 months, then q 21 days for 6 months and q 28 days for 3 months.

PCB - 50 mg/sqm po on days 1 through 5 beginning on completion of radiotherapy and repeated q 14 days for 9 months, then q 21 days for 6 months, then q 28 days for 3 months. Continue therapy for all patients for 1.5 years if possible.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTX - 5 mg vials; VCR - 1 mg vials; PCB - 50 mg tablets.

DATE SUMMARIZED: 11/79

13.0039 PILOT STUDY OF DAILY MULTIFRACTIONATION RADIOTHERAPY AND MISONIDAZOLE FOR HIGH-GRADE MALIGNANT GLIOMA

Ang, K. K., European Org. for Research on Treatment of Cancer, Clinical Coop. Grp. of Radiotherapy, Academisch Ziekenhuis St. Rafael, Radiotherapy Dept., 35 Capucijnenvoer, 3000 Leuven, Belgium

PROTOCOL NUMBER(S) EORTC-22802

OBJECTIVES:

I. Study the tolerance and the effectiveness of a modified radiation therapy schedule combined with high-dose misonidazole for high-grade malignant glioma.

PROTOCOL ENTRY CRITERIA: Patients with histological diagnosis of high-grade malignant glioma after surgical resection or biopsy and patients with recurrence of the same type of tumor after resection. Patients must have normal hematopoietic, renal and hepatic function and a neurological examination that is normal or shows incomplete neurological deficits. Patients must not have been irradiated previously.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy plus Hypoxic Cell Sensitization. Co-60 source; plus Misonidazole, MNI, NSC-261037.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, renal and hepatic function tests; CT scans of brain; electromyograph with determination of conducting velocity of nerves; assessment of clinical neurological status.

END POINTS: Response/remission rate, length of remission, length of survival, recurrence rate.

CURRENT STATUS: 11 patients have been entered as of November 1979.

DOSAGE SCHEDULE:

Radiotherapy. Co-60 source - 600 rads/day given in three 200-rad fractions at 4-hour intervals for 5 days; plus MNI - 1.2 g/sqm po at least 2 hours before each first daily irradiation fraction. Course is repeated after a 2- or 3-week interval. The total first course irradiation dose is pancranial; in the second course, 5 fractions are directed to the entire cranial cavity and 10 fractions are directed to the tumor-bearing area.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

13.0040 ADJUVANT RADIOTHERAPY WITH AND WITHOUT PRIOR RADIOSENSITIZATION WITH MISONIDAZOLE FOR MALIGNANT BRAIN GLIOMA

Calliauw, L., European Org. for Research on Treatment of Cancer, Brain Tumors Cooperative Group, Afdeling Neurochirurgie, St. Jan's Hospital, 8000 Brugge, Belgium

PROTOCOL NUMBER(S) EORTC-26781

OBJECTIVES:

I. Investigate the effects of radiation therapy in combination with the radiosensitizer misonidazole on the duration of the disease-free interval in patients operated for malignant brain glioma.

PROTOCOL ENTRY CRITERIA: Postsurgical patients over 16 years old resected for confirmed malignant glioma, including astrocytoma grade III-IV, malignant ependymoblastoma and astrocytoma, spongioblastoma polare, glioblastoma multiforme, and oligodendroblastoma. Patients must have an expected survival of at least 8 weeks, normal hematopoietic, renal, and hepatic functions, and have no or incomplete and evaluable neurological deficits. Steroid therapy must have been stopped on the 10th day after surgery, anticancer agents prior to surgery, and nitrosourea 4 weeks before radiotherapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy.

Arm II: Single-agent Radiosensitization plus Radiotherapy. Misonidazo le, NSC-261037.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: EEG, isotopic and CT scans.

END POINTS: Recurrence-free interval, relapse rate, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: About 120 patients will be entered.

DOSAGE SCHEDULE:

Arm I: 4950 rad given as 350 rad fractions 3 x/week for 5 weeks to the whole brain, for the first 3 weeks, to tumor site with a 2 cm margin for the last 2 weeks.

Arm II: Misonidazole - 1.3 g/sqm/day po given for the first 3 weeks 4 hours prior to radiotherapy for a total dose of 12 g/sqm. Radiotherapy as in Arm I.

Follow all patients q 3 to 4 weeks until recurrence of neurologic symptoms and until death. Upon relapse, patients may be entered to protocol EORTC-26782.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/79

13.0041 PHASE II POSTOPERATIVE RADIOTHERAPY AND CHEMOTHERAPY WITH CCNU FOR MALIGNANT GLIOMA

Glinski, B., (Krakow 299-00) Instytut Onkologii, Dept. of Radiotherapy, Garncarska 11, 31-115 Krakow, Poland

PROTOCOL NUMBER(S) POL-BN-1

OBJECTIVES:

I. Determine the survival rates, quality of survival, and tolerance of postoperative radiotherapy and chemotherapy with CCNU for malignant brain glioma.

PROTOCOL ENTRY CRITERIA: Patients over 14 years of age with histologically proven malignant glioma. Patients must be in good general and good neurological condition and have received no prior radiotherapy or chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study. Patients are entered following Surgery.

Radiotherapy plus Single-agent Chemotherapy. Co-60 source; CCNU, NSC-79037.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 40 patients are entered as of March 1980; 60 will be entered.

DOSAGE SCHEDULE:

Co-60 - 5000 rads whole brain irradiation through bilateral opposed portals in 25 treatments; plus 1000-rad booster dose in 5 fractions/week. CCNU - 100 mg/sqm po on day 1 q 8 weeks for 6 courses. First course is given while booster irradiation is applied. Patients with disease progression go off study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 10/80

SECTION 14

SOLID TUMORS

RTOG-7923 RADIOTHERAPY WITH PI MESONS ALONE OR WITH CONVENTIONAL RADIOTHERAPY FOR MISCELLANEOUS ADVANCED OR RECURRENT SOLID TUMORS 14.0001

RTOG-7924 RADIOTHERAPY WITH PI MESONS FOR MISCELLANEOUS METASTATIC LESIONS 14.0002

SEG-77ST0102 PHASE II STUDY OF CHEMOTHERAPY WITH ANGUIDINE FOR SOLID TUMORS . 14.0003

SEG-78ST222 PHASE II CHEMOTHERAPY WITH MAYTANSINE FOR REFRACTORY SOLID TUMORS 14.0004

MAYO-800302 DOSE-SEEKING STUDIES WITH VARIOUS COMBINATIONS OF DBD, AMSA AND VP-16 FOR ADVANCED SOLID TUMORS 14.0005

MDAR-196 WHOLE BRAIN RADIOTHERAPY & INTRATHECAL & INTRAVENTRICULAR MTX/THIO/DM FOR MENINGEAL CARCINOMATOSIS IN BREAST CARCINOMA & OTHER SOLID TUMORS 14.0006

MDAR-344 CHEMOTHERAPY WITH THIOTEPA/METHOTREXATE/CITROVORUM FACTOR/DEXAMETHASONE PLUS RADIOTHERAPY FOR MENINGEAL INVOLVEMENT OF SOLID TUMORS 14.0007

NCI-78-C-67 PHASE II CHEMOTHERAPY WITH DICHLOROMETHOTREXATE FOR HEPATOCELLULAR CARCINOMA AND OTHER SOLID TUMORS 14.0008

EORTC-16751 PHASE II STUDY OF CHEMOTHERAPY WITH ANHYDRO-ARABINOSYL-5-FLUOROCYTOSINE FOR SOLID TUMORS 14.0009

SECTION 14

SOLID TUMORS

14.0001 RADIOTHERAPY WITH PI MESONS ALONE OR WITH CONVENTIONAL RADIOTHERAPY FOR MISCELLANEOUS ADVANCED OR RECURRENT SOLID TUMORS

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PROTOCOL NUMBER(S) RTOG-7923

OBJECTIVES:

I. Evaluate tumor response and local and regional control with pion radiation.

II. Evaluate the normal tissue response and tolerance to large field multi-fraction pion therapy alone or as a planned boost to conventional radiotherapy.

III. Evaluate the important aspects of treatment planning and technical aspects of delivering radiotherapy with the maximum therapeutic ratio by minimizing the normal tissue irradiated.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven, locally advanced or recurrent disease not amenable to conventional therapy. Patients must be between 18 and 75 years old, with a Karnofsky performance status of 60 or better and a minimum life expectancy of 3 months.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy: Pion radiation to tumor area.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Opthalmologic exam.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival duration, duration of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Radiotherapy: Pion radiation up to (if combined with conventional Radiotherapy not to exceed) 1500 to 7100 rad in 2 to 8 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 02/80

14.0002 RADIOTHERAPY WITH PI MESONS FOR MISCELLANEOUS METASTATIC LESIONS

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PROTOCOL NUMBER(S) RTOG-7924

OBJECTIVES:

I. Evaluate tumor response to pion radiation.

II. Evaluate normal tissue response and tolerance to multi-fraction pion therapy.

III. Evaluate the important aspects of treatment planning and technical aspects of delivering the radiation with a maximum therapeutic ratio by minimizing the normal tissue volume irradiated.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven metastases from any solid tumor not amenable to conventional therapy. Patients must be between 18 and 75 years old with a Karnofsky performance status of 60 or better. The target lesion must have had no prior radiotherapy and patients must have a minimum life expectancy of 3 months.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy: Pion radiation to a metastatic site.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Opthalmologic exam.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival duration, duration of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Radiotherapy: Pion radiation - 1500 to 7100 rad in 2 to 8 weeks.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 02/80

14.0003 PHASE II STUDY OF CHEMOTHERAPY WITH ANGUIDINE FOR SOLID TUMORS

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-77ST0102; SEG-77ST219

OBJECTIVES:

I. Determine the efficacy of anguidine in a Phase II study of prognostically poor solid tumors that have been untreated or have been refractory to previous therapy.

PROTOCOL ENTRY CRITERIA: Patients at least 18 years old with tissue diagnosis of solid tumor, considered incurable, with at least one measurable lesion other than in bone. (Closed to colorectal patients in October 1978 and to patients with small cell lung cancer and myeloma in January 1980.) A Karnofsky performance status of 40% or higher, recovery from any previous therapy, and adequate hematological, hepatic and renal functions are required.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Anguidine, ANG, NSC-141537.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/regression rate, objective tumor response, toxicity/morbidity of treatment, response duration, survival.

CURRENT STATUS: About 412 patients will be entered in 2 1/3 years.

DOSAGE SCHEDULE:

ANG - 5 mg/sqm iv on days 1 through 4. Repeat course q 28 days for a total of 3 courses. Enter patients with liver involvement or dysfunction at 3 mg/sqm in the 1st course, 4 mg/sqm in the 2nd course, and 5 mg/sqm in the 3rd course, if tolerated. Give a minimum of 3 courses unless toxicity is intolerable. Evaluate patients q 2 weeks, then for responders q 2 months for 1 year, then q 4 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ANG - 10 mg vials

DATE SUMMARIZED: 07/78

PATIENT ACCRUAL: 01521078

14.0004 PHASE II CHEMOTHERAPY WITH MAYTANSINE FOR REFRACTORY SOLID TUMORS

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PROTOCOL NUMBER(S) SEG-78ST222; SEG-78ST0102

OBJECTIVES:

I. Determine the therapeutic efficacy of maytansine in patients who have advanced solid tumors that have become refractory to previous therapy or are untreated but have very poor prognosis.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed measurable solid tumors incurable by surgery, radiotherapy or existing chemotherapy. Patients must have a Karnofsky performance status of at least 40% and must have recovered from previous myelosuppressive therapy. Protocol closed to patients with melanoma in July 1978, patients with colorectal carcinoma in October 1978, and patients with gastrointestinal tumors, myeloma, and lung cancer in January 1980.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Maytansine, MTS, NSC-153858.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum electrolytes, liver and kidney function tests, CEA, SMA-12.

END POINTS: Response/remission rate, survival rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 375-415 patients will be entered.

DOSAGE SCHEDULE:

MTS - 0.5 mg/sqm iv infusion over 2 hours (0.25 mg/sqm for patients with abnormal liver function) on days 1 through 3 q 21 days. Evaluate patients 2 weeks after 2nd course and continue therapy for responders. Escalate patients on lower dose by 20% if no further hepatic damage or significant hematologic toxicity has occurred. Remove from study patients with rapidly progressing disease after one course, or patients with unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MTS - 0.25 mg vials.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00240878

14.0005 DOSE-SEEKING STUDIES WITH VARIOUS COMBINATIONS OF DBD, AMSA AND VP-16 FOR ADVANCED SOLID TUMORS

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PROTOCOL NUMBER(S) MAYO-800302

OBJECTIVES:

I. Conduct dose-seeking studies of the combinations of dibromodulcitol (DBD) plus VP-16213 (VP-16), DBD plus AMSA, and DBD plus VP-16 plus AMSA to determine dosages that will, in the majority of patients treated, produce WBC nadirs less than 2,500 cells/cumm or platelet nadirs less than 100,000 cells/cumm.

PROTOCOL ENTRY CRITERIA: Patients with histologically or cytologically confirmed diagnosis of cancer (other than breast, colon or stomach), with advanced or recurrent disease not amenable to treatment by more conventional means or a higher order protocol. Patients with prior chemotherapy with the protocol drugs are not eligible; those who have received other drugs within the 4 weeks prior to entry are not eligible. Patients must not undergo major surgery within the 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study. Regimens A and B are started simultaneously. After Regimen A is filled (maximum of 12 patients), Regimen B is filled. When Regimen A and B studies are completed, Regimen C will be opened to patient entry.

Regimen A: 2-Drug Combination Chemotherapy, Dibromodulcitol, DBD, NSC-104800; VP-16213, VP-16, NSC-141540.

Regimen B: 2-Drug Combination Chemotherapy. DBD; m-AMSA, AMSA, NSC-249992.

Regimen C: 3-Drug Combination Chemotherapy. DBD; VP-16; AMSA.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Hematologic function tests, renal and hepatic function tests.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Maximum of 12 patients will be entered on Regimen A and 15 on Regimens B and C.

DOSAGE SCHEDULE:

Regimen A: DBD - 75 mg/sqm po on days 1-10, escalate to 100 and 150 mg/sqm, repeat q 4 weeks; VP-16 - 75 mg/sqm iv on days 1-3, escalate to 100 mg/sqm, repeat q 4 weeks.

Regimen B: DBD - 75 mg/sqm po on days 1-10, escalate to 100, 125 and 150 mg/sqm, repeat q 4 weeks; AMSA - 50 mg/sqm iv on day 1, escalate to 75, 100 and 100 mg/sqm, repeat q 4 weeks.

Regimen C: DBD - 50 mg/sqm po on days 1-10, escalate to 75 mg/sqm, repeat q 4 weeks; VP-16 - 50 mg/sqm iv on days 1-3, escalate to 50, 75 and 75 and 75 mg/sqm, repeat q 4 weeks; AMSA - 50 mg/sqm iv on day 1, escalate to 75 mg/sqm, repeat q 4 weeks.

Three patients will be treated at each level on each treatment and observed for a minimum of 3 weeks until either a WBC nadir less than 2,500 or a platelet nadir less than 100;000 is observed. At this point, a minimum of 6 patients will be treated at that level.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DBD - 50 mg tablets; VP-16 - 100 mg ampules.

DATE SUMMARIZED: 06/80

14.0006 WHOLE BRAIN RADIOTHERAPY & INTRATHECAL & INTRAVENTRICULAR MTX/THIO/DM FOR MENINGEAL CARCINOMATOSIS IN BREAST CARCINOMA & OTHER SOLID TUMORS

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PROTOCOL NUMBER(S) MDAR-196; MDA-DT-7660

OBJECTIVES:

I. Determine the efficacy of whole brain irradiation, intrathecal and intraventricular methotrexate and thio-tepa in patients with breast cancer and other solid tumors with CNS disease and meningeal involvement.

II. Determine the qualitative and quantitative toxicity of this regimen.

III. Determine the duration of response and survival.

IV. Evaluate the usefulness of CSF CEA determinations as an indicator of meningeal involvement.

V. Determine prospectively the incidence of meningeal involvement in patients with breast cancer.

PROTOCOL ENTRY CRITERIA: Patients with breast carcinoma and other solid tumors who develop proven meningeal carcinomatosis, and all patients with positive brain scans for mass lesions to determine the incidence of diffuse meningeal involvement with concomitant focal intracerebral lesions.

PROTOCOL OUTLINE: Nonrandomized study.

Induction and Maintenance:

Radiotherapy plus 3-Drug Combination Chemotherapy and Hormone Therapy. Methotrexate, MTX, NSC-740; Citrovorum factor, CF, NSC-3590; Thio-tepa, THIO, NSC-6396; Dexamethasone, DM, NSC-34521.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, duration of response.

CURRENT STATUS: 40 patients will be entered per year.

DOSAGE SCHEDULE:

Induction:

Radiotherapy plus Glyceral - 1.8 gm/kg po in 4 divided doses; continuing for one week following completion of whole-brain Radiotherapy. Give DM - 4 mg po if no clinical improvement. Radiotherapy - 4000 rads over two weeks to whole brain. During Radiotherapy, administer MTX - 25 mg IT twice a week; CF - 6 mg/sqm im given immediately after IT MTX and continue 6 mg/sqm po q 6 hours for 48 hours. Patients with elevated creatinine continue CF for 72 hours.

Insert Ommaya shunt upon completion of whole-brain Radiotherapy in all patients showing peripheral remission (complete or partial).

Continue MTX IT until intraventricular Chemotherapy can be given. Patients who demonstrate progressive neurological deterioration and fail to show greater than 50% reduction in tumor cell count after 4 doses of intraventricular MTX shall receive THIO - 15 mg twice a week.

Maintenance:

THIO or MTX - 25 mg twice a week, intraventricular. Continue until complete response is achieved, then give MTX - 25 mg once a week x 4, then q 2 weeks x 6, then q 6 weeks for one year.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

14.0007 CHEMOTHERAPY WITH THIOTEPA/METHOTREXATE/CITROVORUM FACTOR/DEXAMETHASONE PLUS RADIOTHERAPY FOR MENINGEAL INVOLVEMENT OF SOLID TUMORS

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PROTOCOL NUMBER(S) MDAR-344; MDA-MBDT-7919

OBJECTIVES:

I. Determine the efficacy of the combination of whole brain irradiation, intrathecal and intraventricular methotrexate (MTX)/thiotepa in patients with breast cancer or other solid tumors who develop CNS disease with meningeal involvement.

II. Determine the qualitative and quantitative toxicity of this regimen and the duration of response and of survival of patients receiving this therapy.

III. Evaluate the comparative usefulness of sequential CSF CEA and CSF polyamines in the therapeutic determinations, and of monitoring responses and early relapse of meningeal disease.

PROTOCOL ENTRY CRITERIA: Patients with breast, lung, melanoma or other solid tumors with proven meningeal carcinomatosis who have had no prior meningeal therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: 4-Drug Combination Chemotherapy plus Radiotherapy. Methotrexate, MTX, NSC-740; Thiotepa, NSC-6396; Citrovorum factor, CF, NSC-3590; Dexamethasone, DM, NSC-34521.

Maintenance: 2-Drug Combination Chemotherapy. MTX, Thiotepa.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: CSF CEA, CSF polyamines.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 30 patients will be entered in 1 year.

DOSAGE SCHEDULE:

Induction:

DM - 16 mg/day po in 4 divided doses given q 6 hours until 1 week after completion of whole brain irradiation. Radiotherapy - 3000 rad in 2 weeks to the whole brain. MTX - 20 mg intrathecal (it) - intraventricular (ivent) when Ommaya Shunt in place - twice weekly; Thiotepa - 10 mg it or ivent twice weekly; CF - 6 mg/sqm im directly after MTX, then 24 mg/sqm po in 6 divided doses for 24 hours, for 72 hours for patients with elevated creatinine. Upon completion of whole brain irradiation insert Ommaya Shunt in patients with at least partial response, stable disease or life expectancy over 12 weeks despite progression of systemic disease. Continue intrathecal MTX and Thiotepa until Ommaya Shunt can be used, then continue intraventricular therapy, until complete response is achieved.

Maintenance: Enter complete responders from Induction. Thiotepa -10 mg ivent on day 1; MTX - 20 mg ivent on day 1; both repeated q week for 4 courses, then q 2 weeks for 6 courses, then q 6 weeks for one year.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

14.0008 PHASE II CHEMOTHERAPY WITH DICHLOROMETHOTREXATE FOR HEPATOCELLULAR CARCINOMA AND OTHER SOLID TUMORS

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PROTOCOL NUMBER(S) NCI-78-C-67; NCI-VA-MOB-781

OBJECTIVES:

I. Determine the antitumor activity of dichloromethotrexate in patients with hepatocellular carcinoma and other advanced solid tumors.

II. Determine the dose of dichloromethotrexate that produces acceptable toxicity when given as a weekly 6-hour infusion.

III. Investigate the pharmacokinetics of dichloromethotrexate.

PROTOCOL ENTRY CRITERIA: Patients with pathologically confirmed hepatocellular carcinoma or other carcinoma or solid tumor not amenable to curative surgery or other treatment modality. Disease must be progressive and evaluable. Patients must have a life expectancy of at least 1 month and have adequate bone marrow, kidney, and liver function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dichloromethotrexate, DCM, NSC-29630.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hemogram, SMA-12, SMA-6, chest x-ray, coagulation studies, creatinine clearance, urine protein, serum AFP, liver scan, tumor measurement.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

DCM - 100 mg/sqm/week iv over 6 hours for 2 doses in the first 3 patients, escalating to 200 mg/sqm/week for 2 doses then 400 mg/sqm/week until going off study. The second 3 patients will receive 200 mg/sqm/week escalating at 2-week intervals to 400 and 800 mg/sqm/week, the final dose being maintained until patient goes off study. The next 4 patients will receive 400, then 800, then 1200 mg/sqm/week, escalating at 2-week intervals. Patients with progressive disease after 3 doses of DCM go off study; others continue until onset of progressive disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DCM - 250 mg vials.

DATE SUMMARIZED: 08/80

14.0009 PHASE II STUDY OF CHEMOTHERAPY WITH ANHYDRO-ARABINOSYL-5-FLUOROCYTOSINE FOR SOLID TUMORS

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PROTOCOL NUMBER(S) EORTC-16751

OBJECTIVES:

I. Estimate the response rate to anhydro-arabinosyl-5-fluorocytosine (AAFC) given according to 2 different dosage schedules, in a variety of solid tumors: bronchogenic carcinoma, head and neck squamous cell carcinoma, mammary carcinoma and GI tract including pancreatic carcinoma.

PROTOCOL ENTRY CRITERIA: Patients not suitable for surgery or radiotherapy, with histologically confirmed, measurable bronchogenic small cell carcinoma, head and neck squamous cell carcinoma, GI tract adenocarcinoma (including pancreatic adenocarcinoma or breast adenocarcinoma. Patients must be over 15 years old.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. Anhydro-arabinosyl-5-fluorocytosine, AAFC, NSC-166641.

Arm II: Single-agent Chemotherapy. AAFC - different dose schedules.

STRATIFICATION BY: Participating institutions; tumor site; prior chemotherapy: yes or no.

SPECIAL STUDY PARAMETERS: Bone biopsy with imprints, skeletal survey, isotopic scintigraphy (liver).

END POINTS: Response/remission rate, toxicity/morbidity of treatment, survival rate, duration of survival, objective tumor response, progression/relapse.

CURRENT STATUS: About 200 patients will be entered.

DOSAGE SCHEDULE:

Arm I: AAFC - 15 mg/kg/day iv, for days 1 through 5 q 3 weeks. Evaluate at 6 weeks. Patients with disease progression go off study. Continue therapy in responders and non-responders with 20 mg/kg/day for days 1 through 5 q 3 weeks. Evaluate again q 9 weeks. Patients with no response go off study. Continue therapy in responders until progression.

Arm II: AAFC - 33 mg/kg, iv, weekly for 3 weeks, then 50 mg/kg weekly for the next 3 weeks. Evaluate at 6 weeks. Patients with disease progression go off study. Continue therapy in responders with 66 mg/kg weekly. Evaluate at 9 weeks. Patients with no response go off study. Continue therapy in responders until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: None given.

DATE SUMMARIZED: 01/77

SECTION 15

UNSPECIFIED OR MULTIPLE NEOPLASMS

CCG-061 PHASE II INDUCTION AND MAINTENANCE WITH DIANHYDROGALACTITOL FOR CHILDREN WITH REFRACTORY ACUTE LEUKEMIAS OR SOLID TUMORS ... 15.0001
CCG-861 PHASE II SURGERY, RADIOTHERAPY, AND VBL/BLEO/CACP/ACT-D/CTX/ADR COMBINATION CHEMOTHERAPY FOR PRIMARY OR METASTATIC GERM CELL TUMORS ... 15.0002
CLB-7772 PHASE II CHEMOTHERAPY WITH CHLOROZOTOCIN FOR ADVANCED GASTROINTESTINAL, PANCREATIC, LUNG AND BREAST TUMORS, MELANOMA AND LYMPHOMA ... 15.0003
CLB-7971 PHASE II CHEMOTHERAPY WITH AMSA FOR MELANOMA, OVARIAN AND BREAST CARCINOMA, HYPERNEPHROMA, AND HEPATOMA ... 15.0004
NCOG-0R81 PHASE I-II PILOT OF HEAVY CHARGED PARTICLE RADIOTHERAPY FOR LOCALLY ADVANCED OR RECURRENT CANCER OF VARIOUS SITES AND TYPES ... 15.0005
RTOG-7102 COMPARISON OF SPLIT-COURSE VERSUS CONTINUOUS RADIOTHERAPY FOR CARCINOMA OF THE HEAD AND NECK AND UROGENITAL REGIONS ... 15.0006
RTOG-7806 PHASE I/II STUDY OF RADIOTHERAPY, INTERSTITIAL RADIATION, AND HYPERTHERMIA FOR METASTATIC NEOPLASMS ... 15.0007
RTOG-7813 PHASE I/II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS HALF-BODY RADIOTHERAPY FOR NEOPLASMS WITH MULTIPLE METASTASES ... 15.0008
RTOG-7815 PHASE I/II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS RADIOTHERAPY FOR ADVANCED SOFT TISSUE SARCOMAS OR MELANOMAS ... 15.0009
RTOG-7905 PHASE I/II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS RADIOTHERAPY FOR ADVANCED PELVIC MALIGNANCIES ... 15.0010
RTOG-8003 PHASE III COMPARISON OF RADIATION ALONE VS RADIATION PLUS MISONIDAZOLE IN THE TREATMENT OF LIVER METASTASES ... 15.0011
SEG-78ST250 PHASE II HEMIBODY RADIOTHERAPY FOR DISSEMINATED METASTATIC CARCINOMA OF THE LUNG, BREAST, AND PROSTATE ... 15.0012
SEG-79RLPD267 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE IN REFRACTORY NON-HODGKIN'S LYMPHOMA, HODGKIN'S DISEASE, AND CHRONIC LYMPHOCYTIC LEUKEMIA ... 15.0013
SWOG-7919 PHASE II CHEMOTHERAPY WITH AMSA FOR CHILDREN WITH RESISTANT ACUTE LEUKEMIA AND NON-HODGKIN'S LYMPHOMA IN RELAPSE ... 15.0014
SWOG-7960 PHASE I-II PILOT CHEMOTHERAPY WITH COLCHICINE FOR REFRACTORY HODGKIN'S DISEASE, CHRONIC LYMPHATIC LEUKEMIA, LUNG OR BREAST CANCER ... 15.0015
SWOG-7963 PHASE II PILOT CHEMOTHERAPY WITH M-AMSA FOR METASTATIC MELANOMA, MYELOMA, AND OAT-CELL LUNG AND BREAST CARCINOMA ... 15.0016
SWOG-8017 PHASE II COMBINATION CHEMOTHERAPY WITH ADR/CTX/5-FU/SCZ FOR METASTATIC CARCINOID TUMORS ... 15.0017

SWOG-8067 PHASE I-II CHEMOTHERAPY WITH DHAD FOR CHILDREN WITH SOLID TUMORS AND ACUTE LYMPHOCYTIC LEUKEMIA 15.0018
BCRP-7606 PHASE III CHEMOTHERAPY WITH ADR PLUS CACP FOR GENITOURINARY CARCINOMA AND CANCER OF THE CERVIX AND OVARY 15.0019
BCRP-7714 COMPARISON OF ORAL ANTIBIOTIC COMBINATIONS TO PREVENT INFECTIONS IN RELAPSED LEUKEMIC PATIENTS AND IN OAT CELL CARCINOMA PATIENTS 15.0020
BCRP-7803 PHASE II CIS-PLATINUM CHEMOTHERAPY FOR HEAD/NECK TUMORS, SARCOMAS, OR PRIMARY GASTROINTESTINAL, PULMONARY, OR BREAST MALIGNANCIES 15.0021
BCRP-8014 EMPIRIC ANTIBIOTIC THERAPY FOR FEBRILE GRANULOCYTOPENIC CANCER WITH SUSPECTED INFECTION 15.0022
MAYO-790305 EARLY CLINICAL TRIAL OF BCNU PLUS 6-TG FOR ADVANCED MALIGNANT MELANOMA AND GENITOURINARY TUMORS 15.0023
MAYO-800301 EARLY CLINICAL TRIAL OF COMBINATION CHEMOTHERAPY WITH BCNU/PALA FOR ADVANCED CANCER 15.0024
MAYO-800305/807402 PILOT AND PHASE II COMBINATION CHEMOTHERAPY WITH CTX/ADR/CACP FOR ADVANCED CANCER 15.0025
MDAR-110 PHASE I-II CHEMOTHERAPY WITH STREPTOZOTOCIN FOR LYMPHOMA, HODGKIN'S DISEASE, PANCREATIC AND METASTATIC CARCINOID TUMORS ... 15.0026
MDAR-207 CACP OR CACP/BLEO/MTX WITH OR WITHOUT THYMOSIN IMMUNOTHERAPY FOR ADVANCED HEAD AND NECK CANCER AND GENITOURINARY TUMORS .. 15.0027
MDAR-253 CHEMOTHERAPY WITH FAC (5-FU/ADR/CTX) FOR METASTATIC CARCINOID TUMORS 15.0028
MDAR-266 COMBINATION CHEMOTHERAPY WITH MTX/HC/ARA-C/CF AND RADIOTHERAPY FOR ADULT MENINGEAL LEUKEMIA OR LYMPHOMA 15.0029
MDAR-268 COMBINATION CHEMOTHERAPY WITH CYVADIC (CTX/VCR/ADR/DTIC) FOR UNDIFFERENTIATED MALIGNANT NEOPLASMS 15.0030
MDAR-280 CHEMOTHERAPY WITH AIM (L-ASP/MTX/IPP) FOR REFRACTORY ACUTE LYMPHOBLASTIC AND UNDIFFERENTIATED LEUKEMIA AND MALIGNANT LYMPHOMA 15.0031
MDAR-281 CHEMOTHERAPY WITH ICRF-159 AND CYTOSINE ARABINOSIDE FOR ACUTE LYMPHOCYTIC AND MYELOGENOUS LEUKEMIAS AND MALIGNANT LYMPHOMA 15.0032
MDAR-297 5-FU AND THYMIDINE VS 5-FU ALONE FOR ADENOCARCINOMAS OF THE BREAST, LUNG, OR COLORECTUM AND FOR MALIGNANT MELANOMAS 15.0033
MDAR-334 CHEMOTHERAPY WITH FTORAFUR WITH AND WITHOUT ADR/CTX/CACP FOR METASTATIC ADENOCARCINOMA OF UNKNOWN PRIMARY ORIGIN 15.0034
MDAR-346 PHASE I-II STUDY OF HIGH-DOSE ASCORBIC ACID POTENTIATION OF ALKYLATING AGENTS IN CHILDREN WITH ADVANCED CANCER 15.0035
MDAR-365 SINGLE-AGENT CHEMOTHERAPY WITH DIBROMODULCITOL IN PATIENTS WITH ESOPHAGEAL CARCINOMA AND HEAD AND NECK CANCER 15.0036
MDAR-374 PHASE I-II IMMUNOTHERAPY WITH HUMAN IMMUNE INTERFERON FOR PATIENTS WITH DISSEMINATED CANCER 15.0037
MDAR-391 PHASE I-II CHEMOTHERAPY WITH VP-16213 FOR METASTATIC COLORECTAL CARCINOMA, OAT CELL CARCINOMA OF THE LUNG, AND HEPATOMA 15.0038
MDAR-403 PHASE I-II HEPATIC ARTERIAL INFUSION OF DAVA FOR METASTATIC MELANOMA AND OTHER TUMORS CONFINED TO THE LIVER 15.0039
MDAR-61 CHEMOTHERAPY WITH VCR/CTX/ADR OR ACT-D/DTIC PLUS BCG IMMUNOTHERAPY AND VIRAL ONCOLYSATES FOR ADVANCED SARCOMA AND MELANOMA 15.0040
MSKCC-7010 IMMUNOTHERAPY WITH BCG OR MER-BCG FOR CUTANEOUS METASTASES OF CANCER 15.0041

MSKCC-743	IMMUNOTHERAPY BY INFUSION OF ALLOGENIC LYMPHOCYTES IN PATIENTS WITH ADVANCED CARCINOMA	15.0042
MSKCC-7761	L-10M CHEMO/ENDOTHERAPY FOR ADULT ACUTE LYMPHOBLASTIC LEUKEMIA AND NULL CELL OR T CELL LYMPHOBLASTIC LYMPHOMA	15.0043
MSKCC-7918	PILOT PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED SOLID TUMORS AND MALIGNANT LYMPHOMAS	15.0044
NCI-76-C-63	CRANIAL VAULT RADIOTHERAPY PLUS INTRATHECAL MTX WITH OR WITHOUT IT THIOTEPA FOR MENINGEAL CARCINOMATOSIS	15.0045
NCI-77-C-181	PROSPECTIVE RANDOMIZED TRIAL OF HLA-MATCHED PLATELET TRANSFUSIONS AS SUPPORTIVE THERAPY IN THROMBOCYTOPENIC CANCER PATIENTS	15.0046
NCI-78-C-35	PHASE II IMMUNOTHERAPY WITH ANTI-THYMOCYTE GLOBULIN FOR MALIGNANT LYMPHOMA OR LEUKEMIA	15.0047
NCI-78-C-60	PHASE II CHEMOTHERAPY WITH INTERMITTENT HIGH-DOSE CACP FOR LUNG CANCER AND OTHER TUMORS	15.0048
NCI-78-C-97	PHASE II CHLOROZOTOCIN FOR CARCINOMA OF THE BREAST AND OVARY, MELANOMA, ISLET CELL CARCINOMA, LYMPHOMA, SARCOMA, AND OTHER TUMORS	15.0049
NCI-79-C-105	PILOT STUDY OF WR-2721 FOR BONE MARROW PROTECTION IN PATIENTS WITH ADVANCED CANCER RECEIVING HEMIBODY IRRADIATION	15.0050
NCI-79-C-119	PHASE II CLINICAL TRIAL OF 13-CIS-RETINOIC ACID FOR ADVANCED BREAST CANCER AND OTHER SOLID TUMORS	15.0051
NCI-79-C-60	INTRAVENOUS MISONIDAZOLE AS A RADIOSENSITIZER IN PATIENTS RECEIVING RADIOTHERAPY FOR ADVANCED CANCER	15.0052
NCI-79-C-79	PHASE II AND PHARMACOLOGICAL STUDIES OF INTRAPERITONEAL 5-FU FOR STAGE III OVARIAN CARCINOMA AND SELECTED OTHER TUMORS	15.0053
NCI-79-C-80	PHASE II STUDY OF HUMAN LYMPHOBLASTOID INTERFERON VS STABILIZED POLY I:C FOR ACUTE MYELOCYTIC LEUKEMIA, CLL, AND VARIOUS SOLID TUMORS	15.0054
SFCC-78061	PHASE II EVALUATION OF CHEMOTHERAPY WITH AD-32 FOR PATIENTS WITH MEASURABLE METASTATIC MALIGNANT DISEASE	15.0055
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SECTION 15

UNSPECIFIED OR MULTIPLE NEOPLASMS

15.0001 PHASE II INDUCTION AND MAINTENANCE WITH DIANHYDROGALACTITOL FOR CHILDREN WITH REFRACTORY ACUTE LEUKEMIAS OR SOLID TUMORS

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-061

OBJECTIVES:

I. Determine the therapeutic efficacy of dianhydrogalactitol (DAG) in acute leukemia and solid tumors of childhood.

PROTOCOL ENTRY CRITERIA: Children with acute leukemias or solid tumors resistant to standard therapies who have been off prior radiation or chemotherapy for 2 weeks in the absence of progressive disease, off prior nitrosourea therapy for 6 weeks and have had no exposure to DAG. Patients with acute leukemia must have an M3 marrow, and adequate liver and renal function. Patients with solid tumors must have histiologically confirmed and measurable lesions and adequate bone marrow, liver and renal functions. The study was closed to patients with ALL/AUL in February 1978 and to patients with ANLL in February 1980. The study remains open for solid tumor patients and has first new agent priority for patients with neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, Wilms' tumor, osteosarcoma, and brain tumors.

PROTOCOL OUTLINE: Nonrandomized study.

Induction: Single-agent Chemotherapy. Dianhydrogalactitol, DAG, NSC-132313.

Maintenance: Single-agent Chemotherapy. Enter responders from induction therapy. DAG.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, response/remission duration, objective tumor response, dose response, survival time, survival rate.

CURRENT STATUS: A maximum of 15-30 adequately treated patients in each disease category will be required for statistical validity.

DOSAGE SCHEDULE:

Induction: Enter patients with acute leukemia to Regimen A, patients with solid tumors to Regimen B.

Regimen A: DAG - 50 mg/sqm/day iv on days 1 through 5 q 14 days. Examine bone marrow on day 28 and, if M2, on day 56. If marrow is M1, enter patients to Maintenance.

Regimen B: DAG - 7.5 mg/sqm/day iv on days 1 through 5 q 14 days. Enter patients in complete remission on day 28 or 56, or in partial remission on day 56, to Maintenance.

Remove from study patients with progressive disease following at least 2 courses, without response following 4 courses, or with unacceptable toxicity.

Maintenance: DAG - 50 mg/sqm/day iv on days 1 through 5 q 28 days. Monitor bone marrow of leukemic patients q 2 months. Remove these patients from study if bone marrow status is M3. Remove solid tumor patients from study if recurrent or progressive disease occurs, and remove all patients with unacceptable toxicity from study.

Dosage modifications for toxicity and for prior extensive bone marrow irradiation are given.

DOSAGE FORMS: DAG - 50 mg vials.

DATE SUMMARIZED: 05/78

15.0002 PHASE II SURGERY, RADIOTHERAPY, AND VBL/BLEO/CACP/ACT-D/CTX/ADR COMBINATION CHEMOTHERAPY FOR PRIMARY OR METASTATIC GERM CELL TUMORS

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PROTOCOL NUMBER(S) CCG-861

OBJECTIVES:

I. Determine effectiveness of excision surgery, radiotherapy, plus 6-agent chemotherapy with vinblastine (VBL), bleomycin (BLEO), cis-platinum (CACP), actinomycin-D (ACT-D), cyclophosphamide (CTX), and adriamycin (ADR) for malignant germ cell ovarian tumors in respect to length of disease free interval and percentage of patients having long-term survival.

II. Determine the effectiveness of above treatment for patients with residual or metastatic disease in respect to induction of remission and length of remission period.

III. Examine the relationship between prognosis and age, tumor type, staging and pathology.

IV. Determine whether a single-arm study of an infrequent childhood tumor is practical and produces significant conclusions.

PROTOCOL ENTRY CRITERIA: Patients of any age with biopsy-proven malignant primary or metastatic germ cell tumors of the ovary (Addendum 3, March 1979: of any anatomic site, except intracranial or testicular) who have not had previous treatment with any of the drugs used in this protocol or prior Radiotherapy that would preclude use of radiotherapeutic doses recommended herein. Eligible tumors are embryonal carcinoma, endodermal sinus (yolk sac) tumor, malignant teratoma, choriocarcinoma, teratomas with both immature and embryonal components (Addendum 2, Sept. 1978), as well as combinations of these histologic types.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Surgery. Complete excision of local disease and metastases to the abdominal cavity.

Regimen B: Radiotherapy. Supervoltage.

Regimen C: 6-Drug Combination Chemotherapy. Vinblastine, VBL, NSC-49842, Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875; Actinomycin-D, ACT-D, NSC-3053; Cyclophosphamide CTX, NSC-26271; Adriamycin, ADR, NSC-123127.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum alpha-feto protein, serum chorionic gonadotropin, CEA, audiogram, chest tomograph, IVP, bone scan, skeletal survey, isotopic or CT brain scan, liver-spleen scan, sonogram of tumor mass, CAT or tumor mass.

END POINTS: Survival rate, duration of remission, survival time, survival rate, response/remission rate, toxicity/morbidity of treatment, disease free interval.

CURRENT STATUS: 45 to 80 patients will be entered in 3-4 years.

DOSAGE SCHEDULE:

Regimen A: Radical excision if possible of all areas of tumor involvement in the abdominal cavity. Detailed procedures specific to each of the study tumor situations likely to be encountered are included. Approximately 18 weeks (2 cycles) after initiation of Chemotherapy, perform a second laparotomy on all patients showing complete or partial response in order to assess, remove or identify residual tumor or direct subsequent therapy.

Regimen B: Use only to treat residual or persistent tumor present at time of 'second-look' laparotomy. Give 1500 to 4000 rad depending on tumor site. Treat anterior and posterior fields daily for 5 or 6 days/week. Dosage and fields are detailed for the different areas involved.

Regimen C: Give Chemotherapy in 9-week cycles consisting of 3 subcycles of 3 weeks each, commencing at week 0, 3, and 6. Continue therapy until week 102. Establish by laparotomy after the completion of the second cycle (18 weeks) modifications of the third cycle. VBL - 6.5 mg/sqm iv on day 1 of week 0, 9, 19 and for patients with no evidence of disease at week 18, continue on day 1, weeks 21, 24, 33, 42, 51, 60, 69, 78, 87, 96; BLEO - 15 mg/sqm/day iv continuous infusion for 3 days starting 6 hours after VBL given at weeks 0, 9, 21, 24, 33, 42, 51 and 60 (maximum total dose 360 mg/sqm). CACP - 60 mg/sqm by 8 hours iv infusion with adequate hydration on day 4 after completion of BLEO. Maintain urine output at 150 cc/sqm/hr. If necessary , add an additional 200 mg/kg mannitol to the infusion; and if this fails to increase urine output, give 0.5 mg/kg furosemide by iv bolus. Following completion of CACP infusion, continue iv at twice Maintenance until patients can tolerate oral fluids. Take input-output total q hour, and closely monitor and correct electrolytes to maintain homeostasis. ACT-D - 0.015 mg/kg/day iv push for 5 days starting day 1 of weeks 3, 12, 27, 36, 45, 54, 63, 72, 81, 90 and 99; CTX - 600 mg/sqm/day on day 1 of each weekly course of ACT-D; ADR - 40 mg/sqm/day iv on day 1 of weeks 6, 15, 30, 39, 48, 57, 66, 75, 84, 93, 102. If heart is included in radiation field, maximum total dose is 320 mg/sqm (first 8 weeks).

Remove patients with progressive disease after 24 weeks of therapy as well as patients with recurrent or metastatic disease ater 6 months from study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: VBL - 10 mg ampules; BLEO - 15 unit ampules; CACP -10 mg vials; ACT-D - 5 mg vials; CTX - 100, 200 and 511 mg vials; ADR -10 mg vials.

DATE SUMMARIZED: 05/79

PATIENT ACCRUAL: 00100279

15.0003 PHASE II CHEMOTHERAPY WITH CHLOROZOTOCIN FOR ADVANCED GASTROINTESTINAL, PANCREATIC, LUNG AND BREAST TUMORS, MELANOMA AND LYMPHOMA

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PROTOCOL NUMBER(S) CLB-7772

OBJECTIVES:

I. Study the activity of chlorozotocin against advanced gastrointestinal, pancreatic, lung and breast tumors, melanoma and lymphoma. (Closed to patient entry for those with tumors of colon, rectum, lung (all types), and breast. Addendum 1, October 1979.)

PROTOCOL ENTRY CRITERIA: Patients with advanced measurable, histologically confirmed breast, lung, pancreatic, gastrointestinal tumors, melanoma, Hodgkin's Disease, or lymphosarcoma not amenable to curative surgery or primary radiotherapy. (Study is closed to entry of patients with tumors of colon, rectum, lung, and breast. Addendum 1, October 1979.) (Closed to tumors of the pancreas, melanoma, and non-Hodgkin's lymphoma. Remains open to patients with stomach cancer or Hodgkin's disease. Addendum 2, April 1980.) Prior therapy, which may not have included study agent, must have been completed for at least 2 weeks, with at least partial recovery from resulting marrow toxicity. Patients must have a creatinine clearance of at least 70 cc/mm and a life expectancy of at least one month. First priority given to patients who have not received a nitrosourea.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Liver, kidney function; bone marrow aspiration; urinary protein.

END POINTS: Response/remission rate, duration of response, relapse rate, toxicity/morbidity of treatment, objective tumor response, quality of response, survival.

CURRENT STATUS: 30 patients with the following tumors will be entered: breast, lung, pancreatic, gastrointestinal or melanoma. (Study closed to entry of patients with tumors of colon, rectum, lung, and breast. Addendum 1, October 1979.) who must not have had prior therapy with nitrosoureas including 10 patients without any prior chemotherapy; 40 patients with Hodgkins and 20 patients with lymphosarcoma will be studied. All of these will have had prior chemotherapy, including about 20 patients with Hodgkins who have had prior nitrosourea therapy. Patients will be entered over a period of 2 years.

DOSAGE SCHEDULE:

Chlorozotocin - 120 mg/sqm iv on day 1 (maximum 150 mg/sqm) q 6 weeks for a minimum of 3 courses, increasing to maximum dosage if no response and mild toxicity after the first 2 courses. Remove patients from study if there is no response after 3 courses, or when disease progression or relapse is noted.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLZ - 50 mg vials.

DATE SUMMARIZED: 04/80

PATIENT ACCRUAL: 01211178

15.0004 PHASE II CHEMOTHERAPY WITH AMSA FOR MELANOMA, OVARIAN AND BREAST CARCINOMA, HYPERNEPHROMA, AND HEPATOMA

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PROTOCOL NUMBER(S) CLB-7971

OBJECTIVES:

I. Determine the effect of methanesulfonamide (AMSA) on melanoma, ovarian carcinoma, breast carcinoma, hypernephroma, and hepatoma.

PROTOCOL ENTRY CRITERIA: Patients with projected survival of at least 2 months with histologically confirmed measurable melanoma, ovarian carcinoma, breast carcinoma, hypernephroma, or hepatoma for which no adequate therapy is available. (Only the category of hepatoma remains open for patient entry. Breast category closed by Addendum 1, April 1980; ovary, hypernephroma, and melanoma categories closed by Addendum 2, May 1980.) Patients must have adequate hematologic function, have liver function test values no greater than 3 times normal, and must not be eligible for any applicable currently active protocol.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurement; hematologic, liver and kidney function, electrolytes, and studies as indicated for specific tumor sites, brain scan for symptomatic patients.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: 70 patients will be entered in 2 years, a minimum of 14 per tumor type.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv infusion over 30 to 60 minutes in 300 ml 5% dextrose. Repeat q 3 weeks with increments of 20 mg/sqm to a maximum of 160 mg/sqm or until myelosuppression occurs. Then continue indefinitely for patients with tumor response or stable disease. Remove from study patients with no tumor response or progressive disease after 2 maximum doses.

Dosage modifications for toxicity for patients with prior chemotherapy or with hepatic dysfunction are given.

DOSAGE FORMS: AMSA - 20 and 50 mg vials.

DATE SUMMARIZED: 06/80

UNSPECIFIED OR MULTIPLE NEOPLASMS

15.0005 PHASE I-II PILOT OF HEAVY CHARGED PARTICLE RADIOTHERAPY FOR LOCALLY ADVANCED OR RECURRENT CANCER OF VARIOUS SITES AND TYPES

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PROTOCOL NUMBER(S) NCOG-0R81; RTOG-7911

OBJECTIVES:

I. Evaluate normal tissue tolerance to large field multifraction heavy charged particle radiotherapy of helium, carbon, neon or argon ions.

II. Evaluate local tumor responses and establish the dose range required for tumor control.

III. Continue evaluation and refinement of CT based computerized treatment planning, patient immobilization and large field, charged particle radiotherapeutic treatment techniques.

IV. Make an initial evaluation of which heavy charged particle(s) are suitable for prospective randomized clinical trials (in addition to helium ions).

PROTOCOL ENTRY CRITERIA: Patients with a biopsy proven malignancy of a locally advanced or recurrent stage of any histologic type, of any anatomic site, with poor chance of control with conventional radiotherapy, surgery or chemotherapy. Tumors currently being considered include malignant glioma, carcinomas of the esophagus, pancreas or stomach, soft tissue and bone tumors, and advanced pelvic tumors. Patients must not have had previous radiotherapy to areas overlapping the projected treatment portals, nor evidence of an active second malignancy other than skin cancer. Patients must be over 18 years of age except for helium ion treatment, have a Karnofsky score of 50% or better, and a life expectancy greater than 3 months.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Charged particle beams of helium (230 MeV per nucleon) accelerated at the 184-inch cyclotron or carbon, neon, or argon (250 to 600 MeV per nucleon) accelerated at the Bevalac to the tumor site, adjacent tissue and regional lymph nodes when appropriate.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: CAT scan; liver function tests; as indicated by tumor type, pretreatment staging.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, normal tissue effects, duration of response, length of survival.

CURRENT STATUS: At least 6 patients per tumor site will be entered.

DOSAGE SCHEDULE:

Initial dose of 80% of tissue tolerance dose (TTD 5/5) for the most sensitive critical tissues within the field, in 4 fractions/week - 160 to 250 CoRE (equivalent rad of Cobalt 60 gamma rays)/fraction. Escalate dosage at a rate of 5 to 10% after a minimum of 4 patients per tumor target have been treated at a given dose level. Allow treatment rests up to one week; if longer, total dose may be increased individually.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 07/79

15.0006 COMPARISON OF SPLIT-COURSE VERSUS CONTINUOUS RADIOTHERAPY FOR CARCINOMA OF THE HEAD AND NECK AND UROGENITAL REGIONS

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) RTOG-7102; RTOG-9271

OBJECTIVES:

I. Determine whether split-course radiotherapy is more effective than standard uninterrupted radiotherapy with regard to treatment tolerance, tumor control and curability, for treatment of carcinoma of the base of the tongue, tonsillar fossa, nasopharynx, urinary bladder and uterine cervix.

PROTOCOL ENTRY CRITERIA: Patients with carcinoma of the base of the tongue, tonsillar fossa, nasopharynx, uterine cervix (Stages IIB, IIIA, IIIB and IVA), and urinary bladder, Stage C or DI (American Joint Committee Stages III and IV). Patients must not have adenocarcinoma and must be under 80 years of age. (Protocol closed to patients with carcinoma of the base of the tongue July 1976. Protocol closed to head and neck cases July 1979).

PROTOCOL OUTLINE: Randomized study. Radiotherapy dosage and schedule depends upon site of disease.

Arm I: Split-course Radiotherapy.

Arm II: Continuous Radiotherapy.

All Radiotherapy will be with teletherapy energy of 1 MeV or higher.

STRATIFICATION BY: Anatomical site: head and neck, uterine cervix, urinary bladder; T and N classification or stage; participating institutions.

SPECIAL STUDY PARAMETERS: Symptomatology, tumor response.

END POINTS: Localized recurrence/response rate, frequency of regional and distant metastases, survival rate, duration of survival, toxicity/morbidity of treatment, radiation dosage reduction, immediate and late tissue reactions, time to achieve complete response.

CURRENT STATUS: As of June 1980, 838 patients have been entered.

DOSAGE SCHEDULE:

Arm I: Split-course Radiotherapy.

Patients with head and neck carcinoma receive 6000 rads total dose given over 7 weeks with interval of 3-week rest period. Remove carious teeth 1.5 to 2 weeks prior to Radiotherapy. (Closed July 1979.)

Patients with carcinoma of the uterine cervix receive 5000 rads total dose over 7 weeks with interval of 3-week rest period. Administer intercavitary curie therapy 2 to 3 weeks following external irradiation, 4000 rads calculated at point A from radioactive sources in uterine and vaginal canals using a tandem-colpstat combination. Perform surgical urinary diversion and temporary colostomy where applicable.

Patients with carcinoma of the urinary bladder receive 5500 rads total dose given over 7 weeks with interval of 3-week rest period. Perform surgical urinary diversion where applicable.

Arm II: Continuous Radiotherapy. Rest periods (weekends, etc.) for patients receiving continuous Radiotherapy should not exceed 3 days each.

Patients with head and neck carcinoma receive 6000 to 6600 rads total dose given over 6 to 7 weeks. (Closed 7/79.)

Patients with carcinoma of the uterine cervix receive 5100 rads total dose over 6 weeks. Administer intercavitary curie therapy 2 to 3 weeks following external irradiation, 4000 rads calculated at point A from radioactive sources in uterine and vaginal canals by using a tandem-colpstat combination.

Patients with carcinoma of the urinary bladder receive 6000 rads total dose given over 6 weeks.

Evaluate continuously irradiated patients after 3000 rads have been given and at the completion of radiotherapy. Evaluate split-course patients at end of 1st treatment period, at end of rest period, and at end of 2nd treatment. Follow up all patients q 3 months for 2 years and q 4 months thereafter.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 05/79

15.0007 PHASE I/II STUDY OF RADIOTHERAPY, INTERSTITIAL RADIATION, AND HYPERTHERMIA FOR METASTATIC NEOPLASMS

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PROTOCOL NUMBER(S) RTOG-7806

OBJECTIVES:

I. Investigate the efficacy of clinical heating methods and thermometry for superficial or accessible tumors with microwave of frequencies of either 2450 megahertz or 915 megahertz, ultrasound, and interstitial or externally applied radiofrequencies.

II. Determine the thermal tolerance of tissues and the degree of tumor responses using hyperthermia alone or in combination with radiation.

III. Select optimum heating times, temperatures and methods for future protocols.

PROTOCOL ENTRY CRITERIA: Patients over 18 years of age with histologically confirmed, advanced and incurable malignancy of selected primary types, including carcinomas of the lung, esophagus, pancreas, large bowel, breast, head and neck, bladder, bone or soft tissue sarcomas, or melanoma, and with metastases to the skin, mucosa, subcutaneous tissues or superficial lymph nodes. Patients must have a life expectancy of at least 10 weeks and should not be amenable to more conventional treatment. Multiple lesions are desirable and all lesions must be measurable in at least one plane.

PROTOCOL OUTLINE: Nonrandomized study. In patients with multiple lesions, treat each lesion with a separate therapy.

Regimen A: Radiotherapy. 4-10 MeV electrons or orthovoltage: 125 to 300 KVP.

Regimen B: Interstitial Radiation.

Regimen C: Hyperthermia with or without Radiotherapy. 2450 megahertz microwaves, 915 megahertz microwaves, low frequency current or ultrasound.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Tumor measurements, skin scoring, standard focus photography.

END POINTS: Response/remission rate, objective tumor response, thermal tolerance.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Regimen A: Radiotherapy - Deliver between 200 and 700 rads per fraction in 3 to 12 fractions and allow 48 to 96 hours between each fraction.

Regimen B: Interstitial Radiation - Use biplanar or volume implantations of radium, iridium or other isotopes in the form of needles or wires to deliver low frequency current systems.

Regimen C: Hyperthermia and Radiotherapy - Apply heat at a steady temperature up to 43 degrees C, at the deepest aspect of the tumor for at least one hour each session, or one half hour if above 43 degrees C, for a minimum of 3 sessions. Heat may be coordinated with radiation, before and/or after or simultaneously with Radiotherapy, but allowing no more than 30 minutes between modalities if used in sequence. Heat alone may be used on the tumor tissue.

Thermometry for measurement of tumor and skin temperature is described. Continue all treatment as long as condition of patient permits, and continue tumor measurements until lesions have grown to twice their original size.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 09/78

PATIENT ACCRUAL: 00190179

15.0008 PHASE I/II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS HALF-BODY RADIOTHERAPY FOR NEOPLASMS WITH MULTIPLE METASTASES

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PROTOCOL NUMBER(S) RTOG-7813

OBJECTIVES:

I. Determine the tolerance of misonidazole in a larger group of patients with advanced disease on the basis of experience obtained in the RTOG Phase I/II studies for misonidazole and half-body radiation therapy.

II. Determine the normal tissue tolerance and toxicity following single exposure doses of irradiation, particularly of dose-limiting organs: bone marrow and lung, plus kidney, liver, brain, spinal cord, small bowel, and heart. The tolerance and toxicity are to be determined both in terms of both acute and late normal tissue reactions and damage.

III. Observe the relationship between the dose of 5 g/sqm of misonidazole and the 4-6 hour blood level of the drug.

IV. Determine tumor tissue levels of misonidazole in accessible sites.

V. Establish that the tumor clearance rate, disease-free interval, local-tumor control rate, and tumor-relapse patterns are within the expected ranges for each type of disease.

VI. Lay the basis for a randomized Phase III study of misonidazole and hemibody irradiation in patients with advanced, disseminated disease.

PROTOCOL ENTRY CRITERIA: Patients between 18 and 80 years of age with any confirmed neoplasm, except lymphoma or leukemia, and with multiple metastases to one or more organs. Patients must have disease which is palpable or measurable radiographically and must have a life expectancy of at least 4 months. Patients must have adequate bone marrow, hepatic, renal and pulmonary function and a Karnofsky status of at least 40%. Patients must not have had previous half-body irradiation to the segment being treated in this protocol, or new chemotherapy initiated in the 2 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Radiosensitization plus Half-body Radiotherapy. Misonidazole, NSC-261037, plus megavoltage therapy above 1 MeV.

STRATIFICATION BY: Participating institutions, primary site, histology, metastatic sites, performance status, previous therapy.

SPECIAL STUDY PARAMETERS: Renal and hepatic function tests, serum Misonidazole levels, uric acid, total protein, albumin, alkaline phosphatase, LDH, serum electrolytes, brain or CAT scans, SMA-6, SMA-12.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response, disease-free interval, recurrence rate.

CURRENT STATUS: As of May 1980, 32 patients have been entered.

DOSAGE SCHEDULE:

Misonidazole - 5 gm/sqm po 4 to 6 hours before Radiotherapy (maximum single dose 10 gm). (Misonidazole dosage revised to 4 gm/sqm, April 1979.) Dose can be repeated in 6 to 8 weeks if opposite side is to be irradiated. Radiotherapy - 600 rads delivered in a single fraction to the upper, mid, or lower hemibody at a rate of 15 to 40 rads/minute.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Misonidazole - 500 mg tablets.

DATE SUMMARIZED: 09/78

15.0009 PHASE I/II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS RADIOTHERAPY FOR ADVANCED SOFT TISSUE SARCOMAS OR MELANOMAS

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PROTOCOL NUMBER(S) RTOG-7815

OBJECTIVES:

I. Determine the tolerance of misonidazole in a larger group of patients with less advanced disease based on experience obtained in the RTOG Phase I study.

II. Determine the tolerance of the unusual radiation fractionation scheme proposed in this protocol in terms of acute and late normal tissue reaction and damage.

III. Observe the relationship between the dose of misonidazole in mg/sqm, mg/kg, and the 4-6 hour blood level of misonidazole.

IV. Determine tumor tissue levels of misonidazole in accessible sites.

V. Establish that the tumor clearance rate, disease-free interval, local tumor control rate, and tumor relapse patterns are within the expected ranges for this type and stage of disease.

VI. Lay the basis for a randomized Phase III study of misonidazole in this disease.

PROTOCOL ENTRY CRITERIA: Patients between 18 and 80 years of age with histologically confirmed, advanced, inoperable, locally recurrent or evaluable metastatic Stage III melanoma or Stage IV sarcoma. All patients must have disease which is palpable or measurable radiographically and previously untreated with radiotherapy. Patients must have a life expectancy of at least 4 months, a Karnofsky performance status of at least 50%, adequate blood counts and bone marrow, renal, and hepatic function, and acceptable neurologic status. Bone sarcomas and childhood sarcomas are eligible (Revision, July 1979).

PROTOCOL OUTLINE: Nonrandomized study.

Radiosensitization plus Radiotherapy. Misonidazole, NSC-261037; plus megavoltage irradiation.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Serum level of misonidazole, renal and hepatic function tests, alkaline phosphatase, uric acid, electrolytes, LDH.

END POINTS: Response/remission rate, objective tumor response, disease-free interval, drug clearance rate, regression rate, toxicity/morbidity of treatment.

CURRENT STATUS: 40 patients will be entered.

DOSAGE SCHEDULE: Misonidazole - 2.5 g/sqm (revised to 1.75 g/sqm, July 1979) po 4 to 6 hours before Radiotherapy q 7 days (total cumulative dose 15 g/sqm). Radiotherapy - 700 rad in 6 fractions given q 7 days over 6 to 8 weeks, for a total dose of 4200 rad (revised to 600 rad twice/week q 3 weeks, July 1979). Remove patients from study in the event of unacceptable side effects.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Misonidazole - 500 mg tablets.

DATE SUMMARIZED: 09/79

PATIENT ACCRUAL: 00060179

15.0010 PHASE I/II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS RADIOTHERAPY FOR ADVANCED PELVIC MALIGNANCIES

Brady, L., (215-574-3150) Radiation Therapy Oncology Group,
925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) RTOG-7905

OBJECTIVES:

I. Determine the tolerance of misonidazole (MNI) and the unusual radiation fractionation scheme proposed in terms of acute and late normal tissue reaction and damage.

II. Determine the relationship between dose of MNI and 4 to 6 hour blood levels of MNI.

III. Establish that the tumor clearance rate, disease-free interval, local tumor control rate and tumor relapse patterns are within expected ranges for this type and stage of disease.

IV. Prepare for a randomized Phase III study of MNI in advanced pelvic malignancies.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven, FIGO Stage IV squamous cell or adenocarcinoma of the uterine cervix, uterus, ovary or gastrointestinal tract (or pelvis, per August 1980 revision) not amenable to conventional therapy. Patients must be between 18 and 75 years of age, with a Karnofsky performance status of 50 or better and a minimum life expectancy of 4 months. Patients must have adequate renal and neurologic function and must have had no prior radiotherapy to the target site.

PROTOCOL OUTLINE: Nonrandomized study.

Radiosensitization plus Radiotherapy. Misonidazole, MNI, NSC-261037; Radiotherapy with megavoltage equipment.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: IVP, lymphangiogram, cystoscopy, sigmoidoscopy.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, disease-free interval, tumor relapse pattern, tumor clearance rate.

CURRENT STATUS: 25 patients to be entered in 1 year.

DOSAGE SCHEDULE:

MNI - 4 gm/sqm po 4 to 6 hours prior to Radiotherapy. Repeat q 4 weeks for 3 courses. Radiotherapy - 1000 rads to pelvis. Repeat q 4 weeks for 3 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 02/80

15.0011 PHASE III COMPARISON OF RADIATION ALONE VS RADIATION PLUS MISONIDAZOLE IN THE TREATMENT OF LIVER METASTASES

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925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107,
United States of America

PROTOCOL NUMBER(S) RTOG-8003

OBJECTIVES:

I. Compare the frequency and duration of symptomatic relief in patients with liver metastases from a variety of sites treated by radiotherapy alone vs. radiotherapy plus misonidazole.

II. Compare the frequency and duration of normalization of liver function in these 2 groups.

III. Compare the frequency of decrease in the size of liver metastases by CT scans in the 2 groups.

IV. Evaluate the response for each treatment according to site and histology of the primary, performance status, and tumor volume.

V. Evaluate the foregoing objective with respect to the length of survival.

PROTOCOL ENTRY CRITERIA: Patients with histologic verification of malignancy other than leukemia, myeloma, or lymphoma, and with hepatic metastases as documented by liver scan and/or CT scan. Renal function and IVP must be normal and bone marrow function must be adequate. Patients must be between the ages of 18 and 80 and have a Karnofsky performance status of at least 50 percent. Disease should be measurable by CT scan as well as isotope liver scan or physical examination with measurement of the liver at 3 points. There may have been no chemotherapy within 2 weeks of entry, and patients must have recovered from prior toxic effects of chemotherapy. There may have been no prior irradiation of the liver, and the bilirubin must be less than 1.5 mg percent. Patients must have an acceptable neurologic and metabolic status, and there may be no other symptomatic metastases.

PROTOCOL OUTLINE: Randomized study.

Arm I: Radiotherapy. Co-60 teletherapy or supervoltage energy equipment of 2 MeV or greater.

Arm II: Radiotherapy plus Radiosensitization. Radiotherapy as in Arm I plus Misonidazole, MNI, NSC-261037.

STRATIFICATION BY: Participating institutions, site of primary tumor (breast vs. colon vs. other), Karnofsky performance status (50-60 vs. 70-90), extent of metastases (solitary hepatic without extrahepatic vs. multiple hepatic without extrahepatic metastases vs. solitary or multiple hepatic with extrahepatic metastases).

SPECIAL STUDY PARAMETERS: Liver measurements, neurological exam, performance status, hemogram, liver and renal function tests, CEA, EKG, CT scan of liver.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: About 200 patients are expected to be entered in 2 years.

DOSAGE SCHEDULE:

Arm I: 2100 rads midplane tumor dose delivered in four or five 300-rad fractions per week over 1.5 weeks.

Arm II: Radiation as in Arm I. MNI - 1.5 g/sqm 4 hours prior to each Radiotherapy treatment, total cumulative dose not to exceed 10.5 g/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MNI - 100 and 500 mg capsules.

DATE SUMMARIZED: 08/80

15.0012 PHASE II HEMIBODY RADIOTHERAPY FOR DISSEMINATED METASTATIC CARCINOMA OF THE LUNG, BREAST, AND PROSTATE

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-78ST250

OBJECTIVES:

I. Determine the pain response rate, tumor response rate, and toxicity of a single 600-rad dose of hemibody irradiation in patients with disseminated metastatic malignancy.

PROTOCOL ENTRY CRITERIA: Patients less than 70 years old with multiple bone metastases from a proven primary carcinoma of the lung, breast, or prostate; they must have failed prior chemotherapy and/or hormone therapy. Patients must have received no prior chemotherapy within four weeks preceding present therapy, and previously irradiated areas must be shielded. Patients must have a performance status greater than 10% and adequate bone marrow, renal, hepatic, and pulmonary function.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy. Photon beam of 1.2 MeV or higher.

STRATIFICATION BY: Participating institutions; site of primary tumor: lung, breast, or prostate.

SPECIAL STUDY PARAMETERS: SMA-12; liver, bone and brain scans; pulmonary function tests.

END POINTS: Toxicity/morbidity of treatment, response/remission rate, objective tumor response, performance status, pain relief.

CURRENT STATUS: 15 to 88 patients will be entered in about 2 years.

DOSAGE SCHEDULE:

Radiotherapy - 600 rad single dose to upper hemibody port to include top of iliac crest to above vertex of skull or to lower hemibody port to include top of iliac crest to feet. Rest 6 weeks or until peripheral blood count returns to pretreatment level. Repeat dose to other hemibody volume. Give antiemetic 4 hours prior to irradiation and maintain adequate hydration. Selectively give corticosteroids 24 hours prior to irradiation.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 06/79

15.0013 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE IN REFRACTORY NON-HODGKIN'S LYMPHOMA, HODGKIN'S DISEASE, AND CHRONIC LYMPHOCYTIC LEUKEMIA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Tumor Inst., Room 225, University of Alabama, Birmingham, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-79RLPD267

OBJECTIVES:

I. Determine the response rate for gallium nitrate in refractory non-Hodgkin's lymphoma, Hodgkin's disease and chronic lymphocytic leukemia.

PROTOCOL ENTRY CRITERIA: Patients with incurable, non-responsive, biopsy-proven, measurable Hodgkin's disease, non-Hodgkin's lymphoma or chronic lymphocytic leukemia. Patients must have a minimum life expectancy of 6 weeks, be 18 years old or older and have a Karnofsky performance status of 40 or better. Patients must have failed a higher priority therapy and may not have corticosteroids. Patients must have adequate hepatic, renal, and cardiac function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Gallium nitrate, NSC-15200.

STRATIFICATION: Participating institutions; disease type: Hodgkin's vs. non-Hodgkin's lymphoma, favorable vs. non-Hodgkin's lymphoma, unfavorable vs. chronic lymphocytic leukemia; performance status: 40-60 vs. 70-100.

SPECIAL STUDY PARAMETERS: SMA 12.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 42-118 patients to be entered over 2 to 3 years.

DOSAGE SCHEDULE:

Induction. Gallium nitrate - 700 mg/sqm iv on days 1 and 14. Remove patients with no response after 2 courses. Enter all others to Maintenance after a 2-week rest period.

Maintenance. Gallium nitrate - 700 mg/sqm (escalating to 800 mg/sqm by 50 mg/sqm steps if toxicity permits) iv on day 1. Repeat q 2 weeks until disease progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Gallium nitrate - 100 mg vials.

DATE SUMMARIZED: 02/80

15.0014 PHASE II CHEMOTHERAPY WITH AMSA FOR CHILDREN WITH RESISTANT ACUTE LEUKEMIA AND NON-HODGKIN'S LYMPHOMA IN RELAPSE

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7919

OBJECTIVES:

I. Determine effects of AMSA on children with acute lymphocytic or non-lymphocytic leukemia (ALL or ANLL) and non-Hodgkin's lymphoma (NHL) who are in relapse and are resistant to standard therapy.

PROTOCOL ENTRY CRITERIA: Children under 18 years of age with ALL or ANLL with M3 bone marrow or measurable NHL who are in relapse, resistant to standard forms of therapy, and not eligible for protocols of higher priority. Patients must have a life expectancy of at least 4 weeks, normal liver and kidney function, adequate hematologic function, and no prior therapy with the protocol drug.

PROTOCOL OUTLINE: Randomized study for patients with ALL only. Patients with ANLL enter Arm I; those with NHL enter Arm II.

Arms I, II and III. Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992. Dose variation between arms.

STRATIFICATION: Participating institutions.

SPECIAL STUDY PARAMETERS: Hematologic, liver, and kidney function; bone marrow aspirate and biopsy; tumor measurement.

END POINTS: Response/remission rate, duration of remission, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 108 patients will be entered in 3 years.

DOSAGE SCHEDULE:

Arm I: AMSA - 120 mg/sqm/day iv infusion over at least 1 hr for 5 days.

Arm II: AMSA - 60 mg/sqm/day iv for 10 days.

Arm III: AMSA - 30 mg/sqm/day iv for 5 days.

Repeat courses q 21 to 28 days. For leukemia patients if marrow cellularity decreases to less than 20% after the first course, delay second course until there is definite evidence of increasing leukemic infiltrate in marrow or reappearance of blasts in peripheral blood. If marrow cellularity is over 50% through days 14 to 17, increase dose 25%. Repeat course as soon as leukemic regeneration is unequivocal in patients showing significant reduction in leukemic infiltrates short of remission after first course. If there is no reduction in marrow leukemic infiltrate by day 17 after second course, remove patients from study. If leukemic infiltrate is reduced by each of the first 2 courses, give a third course and continue courses if there is progressive improvement short of complete remission. Patients achieving complete remission or response with granulocyte count exceeding 1500 enter Consolidation.

Consolidation therapy: AMSA - 75 mg/sqm for 5 days for 2 courses; then Maintenance therapy: AMSA - 30 mg/sqm for 5 days q 3 or 4 weeks depending on recovery from myelosuppression. Adjust dose for Maintenance by 20% to maintain nadir of granulocytopenia between 100 and 500/cumm.

Lymphoma patients: Repeat initial therapy q 21 days if patient achieves partial or complete response, and adjust dose as in Maintenance for leukemia patients. Remove from study patients with one or more measurable lesions in progression or with clinical deterioration after 2 courses.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 20 and 75 mg ampules.

DATE SUMMARIZED: 11/79

15.0015 PHASE I-II PILOT CHEMOTHERAPY WITH COLCHICINE FOR REFRACTORY HODGKIN'S DISEASE, CHRONIC LYMPHATIC LEUKEMIA, LUNG OR BREAST CANCER

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Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7960

OBJECTIVES:

I. Determine the maximum dose of colchicine which may be safely administered on a once-a-week basis.

II. Determine the response rate to weekly, intravenous colchicine in each of the tumor types tested (Hodgkin's disease, chronic lymphocytic leukemia, lung and breast carcinoma).

III. Determine quantitative and qualitative toxicity of the drug on this schedule.

PROTOCOL ENTRY CRITERIA: Patients with chronic lymphocytic leukemia (CLL), Hodgkin's disease, breast or lung cancer (small and non-small cell) who have failed on SWOG protocols of higher priority. Patients must have recovered from toxicity of prior therapy, must have a bilirubin of no more than 3 mg%, or creatinine not above 2.5 mg%. Performance status must be 0 to 3, life expectancy at least 6 weeks. Measurable disease is desirable.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Colchicine, NSC-757.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Objective tumor response, response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 120 patients will be entered in 9 months to 2 years.

DOSAGE SCHEDULE:

Colchicine - 3 mg (2 mg if bilirubin above 1 mg% but less than 3 mg%, or if creatinine is more than 1.5 mg% but less than 2.5 mg%) iv given q 7 days. Escalate dose by 1 mg/course until evidence of toxicity or tumor regression. Give at least 4 courses with achievement of some toxicity. Remove from study patients with progressive disease or with unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Colchicine - 0.5 mg/ml solution.

DATE SUMMARIZED: 06/79

15.0016 PHASE II PILOT CHEMOTHERAPY WITH M-AMSA FOR METASTATIC MELANOMA, MYELOMA, AND OAT-CELL LUNG AND BREAST CARCINOMA

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Operations Office, 3500 Rainbow Blvd., Suite 100, Kansas City,
Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7963

OBJECTIVES:

I. Determine the effect on survival and the efficacy of m-AMSA in producing regressions or remissions in patients with mestastatic melanoma, lymphoma (Protocol closed to lymphoma patients; those eligible will be registered on SWOG-7918. July, 1979), myeloma, metastatic oat-cell lung carcinoma, and metastatic breast cancer, all resistant to standard chemotherapies.

II. Correlate in vitro m-AMSA sensitivities in the tumor stem cell colony drug system and in vivo m-AMSA activity in these patients.

PROTOCOL ENTRY CRITERIA: Patients with measurable disease of histologically confirmed melanoma, myeloma, breast carcinoma, lymphoma (closed to lymphoma patients, July 1979) or oat-cell carcinoma of the lung, refractory to standard therapies, with a life expectancy of at least 6 weeks. Patients must have adequate hematologic functions and must have recovered from the toxicities of any prior therapy. Poor-risk patients (PRP) are defined as over 65 years old, who have had prior whole abdominal or pelvic radiation, severe myelosuppression with prior chemotherapy, or wbc below 3, 500 and/or platelets below 100,000.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: For myeloma patients only: Total serum proteins, serum electrophoresis, antigenic typing of myeloma protein by immunoelectrophoresis, immunoglobulin quantification, urinary proteins, iodinated-albumin plasma volume.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, relapse rate.

CURRENT STATUS: At least 70 patients will be entered.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm iv q 3 to 4 weeks for good-risk patients if hematologic status is adequate and liver functions have returned to normal. Reduce dosage to 90 mg/sqm for PRP or patients with abnormal liver function and bilirubin between 1.2 and 3.0 mg%. Reduce dosage to 60 mg/sqm for patients with bilirubin above 3 mg% and/or alkaline phosphatase and SGOT more than 3 times normal. Give a minimum of 2 courses for an adequate trial. Remove from study patients unable to tolerate the lowest dose levels, patients with sustained hepatic toxicity or patients with increasing or unsatisfactory stable disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 06/79

15.0017 PHASE II COMBINATION CHEMOTHERAPY WITH ADR/CTX/5-FU/SCZ FOR METASTATIC CARCINOID TUMORS

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Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103,
United States of America
PROTOCOL NUMBER(S) SWOG-8017

OBJECTIVES:

I. Determine whether combination chemotherapy employing 5-fluorouracil (5-FU), cyclophosphamide (CTX), adriamycin (ADR), and streptozotocin (SCZ), is effective in the management of metastatic carcinoid tumors.

II. Study the duration of survival of patients with metastatic carcinoid tumor treated with combination chemotherapy regimens.

III. Provide further information concerning the response and/or survival of patients with metastatic carcinoid originating in different sites and having different metastatic patterns.

PROTOCOL ENTRY CRITERIA: Patients with biopsy-proven carcinoid tumor, not amenable to further surgery. Disease must be objectively measurable, either by a measurable lesion or significant biochemical abnormality. Patients must possess significant symptoms or disability resulting from their disease. Patients must have an estimated life expectancy of at least 6 weeks. Patients must possess adequate hematologic and renal functions; those with elevated liver function are eligible. Patients must have no previous malignancy (except nonmelanomatous skin cancer or in situ carcinoma of the cervix). Patients may not have received any chemotherapy or radiotherapy within the 6 weeks prior to entry. At the time of entry, patients should be 3 weeks post any major surgical procedure. Pathology review is mandatory.

PROTOCOL OUTLINE: Nonrandomized study. Patients with cardiac disease enter Regimen B; all others enter Regimen A.

Regimen A: 4-Drug Combination Chemotherapy. FAC-S: 5-Fluorouracil, 5-FU, NSC-19893; Streptozotocin, SCZ, NSC-85998; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271.

Regimen B: 3-Drug Combination Chemotherapy. 5-FU; SCZ; CTX.

STRATIFICATION BY: Participating institutions; prognostic risk status: good vs. poor.

SPECIAL STUDY PARAMETERS: Pathology review, endocrine hyperfunction (24-hour urinary 5-HIAA), blood serotonin and histamine levels, cardiac scan, ECHO, EKG, chest x-ray.

END POINTS: Response/remission rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 50 patients will be entered over 2 years.

DOSAGE SCHEDULE:

Poor-risk patients (those over 70 years of age or those with hepatic abnormalities, urinary 5-HIAA excretion greater than 150 mg/24 hours, carcinoid syndrome, extensive prior radiotherapy or bone marrow involvement) receive the reduced drug dose shown within parentheses.

Regimen A: 5-FU - 400 (300) mg/sqm iv on days 1 and 8; SCZ - 400 (200) mg/sqm iv on days 1 and 8; ADR - 30 (15) mg/sqm iv on day 1; CTX - 75 (50) mg/sqm po on days 1 through 14. Repeat at 28-day intervals as tolerated.

Regimen B: 5-FU - 600 (400) mg/sqm iv on days 1 and 8; SCZ - 600 (400) mg/sqm iv on days 1 and 8; CTX - 100 (75) mg/sqm po on days 1 through 14. Repeat at 28-day intervals as tolerated.

Patients with progressive disease after 2 cycles go off study. Those with stable disease, PR or CR continue therapy until relapse. Those who develop uncontrollable toxicity go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: ADR - 10 and 50 mg ampules; CTX - 100, 200 and 500 mg vials and 50 mg tablets; 5-FU - 500 mg ampules; SCZ - 1 g ampules.

DATE SUMMARIZED: 10/80

15.0018 PHASE I-II CHEMOTHERAPY WITH DHAD FOR CHILDREN WITH SOLID TUMORS AND ACUTE LYMPHOCYTIC LEUKEMIA

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PROTOCOL NUMBER(S) SWOG-8067

OBJECTIVES:

I. Determine the toxicity and maximum tolerated doses of dihydroxyanthracenedione (DHAD) in an abbreviated Phase I trial in children with advanced malignant disease unresponsive to conventional therapy.

II. Determine the response rate to DHAD administered to children with acute lymphoblastic leukemia (ALL) in relapse (equal to or more than 25 percent blasts in the bone marrow) resistant to conventional therapy.

III. Continue evaluating the qualitative and quantitative toxicity of DHAD in children with ALL.

PROTOCOL ENTRY CRITERIA: Phase I. Children with advanced malignant disease not amenable to standard therapy. Patients must have a life expectancy of at least 6 weeks; nutritional status must be adequate and there must be no uncontrolled serious infection. Prior therapy is limited to prednisone for one or more weeks with evidence of recovery and to anthracyclines and nitrosoureas for three or more weeks. There must be normal hepatic and renal functions. Phase II. Children with ALL with an M3 marrow resistant to standard therapy. Patients must have a life expectancy of at least 3 weeks and have normal hepatic and renal functions. Prior therapy restrictions are the same as for Phase I part of the protocol.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dihydroxyanthracenedione, DHAD, NSC-301739.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: EKG; echocardiogram; hematologic, renal and hepatic function tests.

END POINTS: Response/remission rate, recurrence rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: A minimum of 14 patients will be entered for pilot studies after which 2 patients per month will be entered.

DOSAGE SCHEDULE:

Phase I: DHAD - 16 mg/sqm through a free-running iv over 30 minutes, q 3 weeks, given to first 3 patients. The next 3 patients will be given 18 mg/sqm if no undue myelosuppression or other significant toxicity occurs in first 3 patients. Similarly, the succeeding dose level will be 20 mg/sqm. Further dose escalation will be per the coordinator. At least 6 patients with ALL and 6 with solid tumors will be entered at the maximum tolerated dose level before Phase II trial is initiated.

Phase II: DHAD is given as in Phase I, starting dose to be determined in the Phase I trial. Bone marrow status is determined at 3 weeks; patients with progressive disease go off study. Patients with partial response will repeat DHAD course until complete remission or progressive disease.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DHAD - 2.5 and 5 mg ampules.

DATE SUMMARIZED: 10/80

15.0019 PHASE III CHEMOTHERAPY WITH ADR PLUS CACP FOR GENITOURINARY CARCINOMA AND CANCER OF THE CERVIX AND OVARY

Klein, M. E., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7606

OBJECTIVES:

I. Assess the clinical efficacy of adriamycin plus cis-platinum in patients with cancer of testicle, bladder, prostate, ureter, renal pelvis, cervix, or ovary.

II. Evaluate the effectiveness of hydration, mannitol, and furosemide in ameliorating the renal toxicity of cis-platinum.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven carcinoma of the testicle, bladder, prostate, renal pelvis, cervix, or ovary who have not previously received adriamycin or cis-platinum. Patients may not have a history of congestive heart failure or severe hypertension. Patients must have measurable disease.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematological parameters, CEA and alpha-fetoprotein (if abnormal prior to entry), renal function studies, chest x-ray, audiogram, chorionic gonadotropin if previously abnormal, appropriate follow-up urological and gynecologic procedures.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

ADR - 60 mg/sqm iv on day 1. CACP - 75 mg/sqm iv in a 2-liter iv infusion over 6-8 hours with prehydration and concomitant mannitol-lasix induced diuresis on days 1 and 8. Repeat course at 21-day intervals. Continue treatment for a minimum of 3 courses in the absence of progression. Two additional courses should be given after CR (minimum of 6 courses). Patients who progress after 2 courses, have a PR but stabilize with residual disease, or show no change after 3 courses of Induction should go off protocol.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

15.0020 COMPARISON OF ORAL ANTIBIOTIC COMBINATIONS TO PREVENT INFECTIONS IN RELAPSED LEUKEMIC PATIENTS AND IN OAT CELL CARCINOMA PATIENTS

Love, L. J., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7714

OBJECTIVES:

I. Compare trimethoprim/sulfamethoxazole (TMP/SMZ) plus amphotericin in orobase vs. gentamicin/vancomycin/nystatin/betadine (GVN) for the ability to prevent infections in granulocytopenic leukemic patients.

II. Compare TMP/SMZ vs. placebo as a means of preventing infections in oat cell carcinoma patients undergoing their first two courses of chemotherapy.

III. Challenge the concept of total enteric flora suppression as a means of infection prevention in granulocytopenic patients.

IV. Determine whether bacteremias, clinically documented infections, and nonbacteremic microbiologically documented infections in the patients taking TMP/SMZ will be reduced to a level equal to or lower than that currently found in patients on GVN.

V. Determine whether Candida colonization and infections will be comparable in the two groups.

VI. Determine patient acceptance of the two regimens.

PROTOCOL ENTRY CRITERIA: Patients with acute leukemia in relapse or chronic myeloid leukemia in blast crisis who are to begin Induction chemotherapy. Leukemic patients must have an expected granulocytopenic period of at least 7 days. Patients with oat cell carcinoma who are about to undergo their first course of Induction therapy.

PROTOCOL OUTLINE: Randomized study. Randomize leukemic patients to Arms I and II and oat cell carcinoma patients to Arms III or IV. Leukemic patients concurrently begin Induction chemotherapy (no details given); oat cell carcinoma patients are concurrently treated on BCRP protocol 7705.

Arm I: Antibiotic Therapy. Gentamicin, GTM; Nystatin, NYS, Vancomycin, VCM; Betadine, BET.

Arm II: Antibiotic Therapy. Trimethoprim, TMP, NSC-106568; Sulfamethoxazole, SMZ; Amphotericin, APT, NSC-527017.

Arm III: Antibiotic Therapy. TMP; SMZ.

Arm IV: Placebo.

STRATIFICATION BY: Cancer type (leukemia vs. oat cell carcinoma).

SPECIAL STUDY PARAMETERS: Surveillance cultures.

END POINTS: Rate of development of infections.

CURRENT STATUS: About 20 patients will be allocated to each group.

DOSAGE SCHEDULE:

Arm I: GTM suspension - 1.2 g po/day in 6 divided doses; NYS tablets - 24 million U/day po in 6 divided doses; NYS suspension - 6 million U/day po in 6 divided doses; VCM - 3 g/day po in 6 divided doses; BET - 120 ml/day in 6 divided doses, administered 2 hours after other agents. NYS treatment begins 24 hours prior to antibiotics.

Arm II: TMP - 320 mg/day po in 2 divided doses; SMZ - 1.6 g/day po in 2 divided doses; APT in Orobase - 1 g applied to the inner and outer surfaces of the upper and lower gums q 4 hours and at bedtime. APT treatment to begin 24 hours prior to TMP and SMZ.

Continue treatment of leukemic patients as long as poly count is less than 1000.

Arm III: TMP and SMZ as in Arm II. Begin on day 1 of the first course of Chemotherapy and continue until day 1 of the third course.

Arm IV: Placebo - 2 tablets/day in divided doses beginning on day 1 of the first course of Chemotherapy and continuing until day 1 of the third course.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

15.0021 PHASE II CIS-PLATINUM CHEMOTHERAPY FOR HEAD/NECK TUMORS, SARCOMAS, OR PRIMARY GASTROINTESTINAL, PULMONARY, OR BREAST MALIGNANCIES

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PROTOCOL NUMBER(S) BCRP-7803

OBJECTIVES:

I. Determine the efficacy of high dose cis-platinum in patients with head and neck tumors, sarcomas, or primary malignancies of gastrointestinal, pulmonary, or breast origin.

II. Compare the effectiveness of hydration plus Lasix to that of hydration plus mannitol in ameliorating renal toxicity associated with the chemotherapeutic agent.

III. Determine peak blood levels and serum half-lives of cis-platinum.

IV. Evaluate fully any neurotoxicities caused by cis-platinum.

PROTOCOL ENTRY CRITERIA: Patients with biopsy proven head and neck tumors, sarcomas, or primary malignancies of gastrointestinal, pulmonary, or breast origin who have not previously received cis-platinum and for whom no other treatment exists. Patients must have adequate renal function, measurable disease, and a prognosis of at least 1 month. Patients must be able to tolerate a fluid load and may not be over the age of 75.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875; plus Lasix-induced diuresis.

Arm II: Single-agent Chemotherapy. CACP; plus Mannitol-induced diuresis, Mannitol, NSC-9256.

STRATIFICATION BY: None specified.

SPECIAL STUDY PARAMETERS: EMG, audiogram, liver and bone scans where indicated, nerve conduction velocities, serum creatinine and creatinine clearance, hematologic parameters.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CACP - 100 mg/sqm in 6-hour iv infusion after prehydration and with concomitant diuresis. Lasix - 40 mg iv push during CACP administration. Repeat courses q 21 days. Continue treatment of complete responders until relapse. Partial and mixed responders continue therapy as long as improvement continues or until progression. Patients with stable disease for at least 2 courses go off protocol and patients with progressive disease over 1 or more courses go off protocol.

Arm II: CACP as in Arm I; Mannitol - 37.5 g iv push during CACP administration.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

15.0022 EMPIRIC ANTIBIOTIC THERAPY FOR FEBRILE GRANULOCYTOPENIC CANCER WITH SUSPECTED INFECTION

DeJongh, C. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-8014

OBJECTIVES:

I. Determine whether the combinations of azlocillin plus amikacin or cefotaxime plus amikacin are more efficacious, less toxic, or both, than the current standard regimen of ticarcillin plus amikacin for empiric antimicrobial therapy of the febrile granulocytopenic patient with cancer.

II. Determine whether a standard course of antibiotic therapy (about one week) is adequate for the persistently granulocytopenic patient with apparently resolved infection, whether antibiotics should be continued until return of circulating granulocytes, and whether prolonged antibiotic therapy predisposes to additional infections or greater drug-related toxicities.

III. Determine whether the patient with persistent fever and granulocytopenia and no apparent site of infection benefits from the addition of empiric amphotericin-B on the assumption that occult fungal infection exists.

PROTOCOL ENTRY CRITERIA: Cancer patients with an absolute granulocyte count of less than 1000/microliter and a temperature above 38.5 degrees C (100.6 degrees F). If the temperature is strongly felt to be due to recently administered blood products or chemotherapy, or if the infecting organism is known, the patient will not be entered. Patients may repeat the study provided 5 days have elapsed between the end of one therapy and the beginning of the next.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Antibiotic Therapy. Ticarcillin; Amikacin.

Arm II: 2-Drug Antibiotic Therapy. Azlocillin; Amikacin.

Arm III: 2-Drug Antibiotic Therapy. Cefotaxime; Amikacin.

Arm IV: 3-Drug Antibiotic Therapy. Two drugs from Arm I, II, or III; plus Amphotericin-B, NSC-527017.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Kirby-Bauer pathogen test; serum antibiotic and bactericidal assays; virologic and mycologic samples.

END POINTS: Duration of response, disease-free interval.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: Ticarcillin - 300 mg/kg/day iv infusion over 15 minutes in 4 divided doses; Amikacin - 15 mg/kg/day in 4 divided doses.

Arm II: Azlocillin - 300 mg/kg/day iv infusion over 15 minutes in 4 divided doses; Amikacin - 15 mg/kg/day in 4 divided doses.

Arm III: Cefotaxime - 100 mg/kg/day iv infusion over 15 minutes in 4 divided doses; Amikacin - 15 mg/kg/day in 4 divided doses.

Evaluate patients in Arms I, II and III on day 4. Patients with improving defined infection and polynuclear neutrophil leukocytes (PMN) greater than 100/microliter continue treatment for a total of 9 days; those with PMN levels less than 100/microliter will be rerandomized to treatment either for 9 days or until PMN levels exceed 1000/microliter (maximum 21 days). Patients with defined infection not improving will be considered for other therapies. Patients with no defined infection, with continued fever and granulocytopenia will be rerandomized either to continued protocol antibiotics or to Arm IV. Patients with doubtful infection will go off study on day 4.

Arm IV: Continue protocol antibiotics; plus Amphotericin - 1 mg initially iv infusion over minimum of 4 hours, followed by progressive doses to achieve 1 mg/kg in first 24 hours. Thereafter, 1 mg/kg on alternate days for total dose of at least 500 mg.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

15.0023 EARLY CLINICAL TRIAL OF BCNU PLUS 6-TG FOR ADVANCED MALIGNANT MELANOMA AND GENITOURINARY TUMORS

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-790305

OBJECTIVES:

I. Determine a dose schedule of BCNU plus 6-thioguanine in patients with advanced malignant melanoma and genitourinary tumors that produces definite but tolerable hematologic toxicity defined as a WBC nadir between 1500 and 2500 cells/cumm and a platelet nadir between 75,000 and 100,000/cumm.

PROTOCOL ENTRY CRITERIA: Patients with histologic or cytologic proof of advanced malignant melanoma or genitourinary cancer for which neither surgery nor radiation therapy nor known chemotherapy would offer significant benefit. Patients may not be eligible for a higher order protocol and must have proven unresectable, residual, or metastatic cancer whether or not it is measurable or evaluable. Patients must have adequate bone marrow, liver, and kidney function and must have an ECOG status better than 4. Patients may not have undergone major surgery or received chemotherapy within the 3 weeks prior to entry (6 weeks for chemotherapy with mitomycin-C). Nitrosoureas may not have been taken at any time, and the patient must not have received radiotherapy to more than 15 percent of functioning bone marrow within a 30-day period.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. BCNU, NSC-409962; 6-Thioguanine, TG, NSC-752.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Tumor measurement, hematologic parameters, blood chemistries, chest x-ray.

END POINTS: Response/remission rate, duration of response, interval to progression, survival, toxicity/morbidity of treatment.

CURRENT STATUS: About 15-20 patients will be entered.

DOSAGE SCHEDULE:

TG - 250 mg/sqm iv over 30 minutes escalated in groups of 3 patients to 375, 550, and 700 mg/sqm; BCNU - 70 mg/sqm iv over 1 hour beginning 1 hour after TG, escalated in groups of 3 patients to 100, 150, and 200 mg/sqm. Retreatment interval is approximately 6 weeks. Three patients are followed for 6 weeks at each dose level before the subsequent level is opened. If dose-limiting toxicity is seen in a patient, 3 additional patients will be entered at that level; if no dose-limiting toxicity is observed in these additional patients, dose escalation is continued. No patient will be treated at more than one dose level.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; TG - 75 mg vials.

DATE SUMMARIZED: 07/80

15.0024 EARLY CLINICAL TRIAL OF COMBINATION CHEMOTHERAPY WITH BCNU/PALA FOR ADVANCED CANCER

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-800301

OBJECTIVES:

I. Determine a dose schedule for the combination of PALA and BCNU that produces definite, but tolerable, hematologic toxicity.

PROTOCOL ENTRY CRITERIA: Patients with histologic or cytologic diagnosis of unresectable, residual, or metastatic advanced stage cancer for which neither surgery nor radiotherapy nor known chemotherapy would offer greater benefit than that anticipated on this protocol. Patients must have an ECOG performance status under 4, adequate hematologic and renal function, and adequate veins. Patients must have no previous treatment with nitrosoureas or PALA and must not have received radiotherapy so as to compromise bone marrow function. Patients must not receive chemotherapy within the 3 weeks prior to entry (6 weeks for mitomycin-C).

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. BCNU, NSC-409962; PALA, NSC-224131.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Hematologic function tests, tumor measurements, renal and hepatic function tests, chest x-ray.

END POINTS: Toxicity/morbidity of treatment, response rate, objective tumor response, survival.

CURRENT STATUS: Approximately 15-20 patients will be entered.

DOSAGE SCHEDULE:

Initial dose level: PALA - 5.0 g/sqm iv over 90 minutes; BCNU - 40 mg/sqm iv over 60 minutes given 30 minutes after the completion of PALA infusion. Escalation level 1: BCNU - 80 mg/sqm iv over 60 minutes, 30 minutes after the completion of PALA (dose remains 5.0 g/sqm at all escalation levels) infusion. Escalation level 2: BCNU - 150 mg/sqm. Escalation level 3: BCNU - 200 mg/sqm. Escalation level 4: BCNU - 240 mg/sqm. For subsequent dose levels, BCNU dose is increased by 10 percent. Course is repeated q 6 weeks. Three patients will be entered at each dose level and followed for 6 weeks before the subsequent escalation dose level is opened. Patients showing regression or stable disease and acceptable toxicity continue treatment at the same dose level; those showing regression and unacceptable toxicity are treated at an appropriately reduced dose. Patients who show progression go off study. At any escalation level, when one patient demonstrates potentially dose-limiting toxicity, 3 additional patients will be entered at that level. If dose-limiting toxicity is not seen in any of these, escalation will continue. No one patient will receive dosage escalation.

Dosage modifications for toxicity are given.

DOSAGE FORMS: BCNU - 100 mg vials; PALA - 1000 mg vials.

DATE SUMMARIZED: 10/80

15.0025 PILOT AND PHASE II COMBINATION CHEMOTHERAPY WITH CTX/ADR/CACP FOR ADVANCED CANCER

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 First Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-800305/807402

OBJECTIVES:

I. Determine in a Pilot study (MAYO-800305) a dose schedule of the combination cyclophosphamide and adriamycin with a 24-hour cis-platinum infusion that produces definite, but tolerable, hematologic toxicity.

II. Assess in a Phase II study (MAYO-807402) the antitumor activity and toxicity of this regimen in patients with advanced head and neck cancer.

PROTOCOL ENTRY CRITERIA: Patients with histologic or cytologic diagnosis of cancer (unresectable, residual, or metastatic) of advanced stage for which neither surgery nor radiation therapy nor known chemotherapy would offer significant benefit are considered in the Pilot study. Patients with histologically proven carcinoma arising from the upper respiratory or alimentary passages of the head and neck or from accessory glands lying contiguous to these passages, measurable or evaluable metastatic disease that is incurable by surgery or radiation therapy are considered in the Phase II study. Patients must have a WBC greater than 4000 and/or platelets greater than 130,000, serum creatinine less than 1.9 mg/dl, ECOG performance better than 4, adequate veins, and adequate cardiac function. Patients must have had no chemotherapy or surgery for 3 weeks prior to entry. Patients must not have received radiation so as to compromise bone marrow function or received prior treatment with the protocol drugs.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION BY: Cancer type: squamous cell vs. other; histologic grade: 1, 2 vs. 3, 4; previous treatment: surgery vs. radiation vs. other; performance score (ECOG): 0, 1 vs. 2, 3.

SPECIAL STUDY PARAMETERS: Tumor measurements; hematologic, renal, and hepatic function tests; PA chest x-ray; stat creatinine.

END POINTS: Response/remission rate, duration of regression, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 15 patients will be entered, 3 at each dose level.

DOSAGE SCHEDULE:

CTX - 200 mg/sqm iv push; ADR - 30 mg/sqm iv push; CACP - 90 mg/sqm iv infusion over 24 hours with 12.5 g mannitol. Escalate to CTX - 300 mg/sqm iv push; ADR - 30 mg/sqm iv push; CACP - unchanged. Escalate to CTX - 300 m/sqm iv push; ADR - 40 mg/sqm iv push; CACP - unchanged. Escalate to CTX - 400 mg/sqm iv push; ADR - 40 mg/sqm iv push; CACP - unchanged. Thereafter, begin escalating CTX and ADR doses by 10 percent; CACP dose level remains constant. Three patients will be entered at each dose level and followed for 4 weeks before the subsequent escalation level is opened. Escalation will continue until limiting toxicity is observed in more than one patient.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CTX - 100, 200, and 500 mg vials; ADR - 10 and 50 mg vials; CACP - 10 mg vials.

DATE SUMMARIZED: 09/80

15.0026 PHASE I-II CHEMOTHERAPY WITH STREPTOZOTOCIN FOR LYMPHOMA, HODGKIN'S DISEASE, PANCREATIC AND METASTATIC CARCINOID TUMORS

Rodriguez, V., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-110; MDA-DT-7541

OBJECTIVES:

I. Investigate the efficacy of streptozotocin by prolonged iv infusion and attempt to reduce the drug-related nephrotoxicity.

II. Evaluate the activity of SZC in patients with advanced lymphoma who have progressed to higher priority chemotherapy, particularly patients with hypocellular bone marrow who cannot tolerate myelosuppressive therapy.

PROTOCOL ENTRY CRITERIA: Patients with malignant lymphoma or Hodgkin's disease and metastatic carcinoid tumors, and pancreatic islet cell tumors, who have no proteinuria and a creatinine clearance above 60 cc/min.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Streptozotocin, SZC, NSC-85998.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 15 patients will be entered.

DOSAGE SCHEDULE:

SZC - 0.5 mg/sqm/day iv x 3 days and q 3 weeks, provided toxicity effects have disappeared. No dose escalation will be allowed. Maintain responders who achieve remission on best tolerated dose.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 02/77

15.0027 CACP OR CACP/BLEO/MTX WITH OR WITHOUT THYMOSIN IMMUNOTHERAPY FOR ADVANCED HEAD AND NECK CANCER AND GENITOURINARY TUMORS

Murphy, W. K., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-207; MDA-DT-7664

OBJECTIVES: (This protocol replaces MDAR-75)

I. Determine the efficacy of cis-platinum (CACP) vs. CACP/methotrexate (MTX)/Bleomycin (BLEO), both with or without immunotherapy with thymosin for advanced head and neck squamous cell cancer, testicular cancer, prostate cancer, and bladder cancer.

II. Study the pharmacokinetics of CACP.

III. Determine the kinetic response of tumor and bone marrow in patients receiving CACP.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven, measurable, advanced head and neck squamous cell carcinoma (including lymphoepithelioma) and other miscellaneous tumors of the testis, prostate, and bladder not amenable to curative surgery or radiotherapy, including untreated patients and patients who have failed previous therapy. Patients must have unimpaired and adequate renal function, adequate bone marrow reserve, no uropathic obstruction, and an expected survival of 8 weeks; there must be no concomitant use of nephrotoxic drugs.

PROTOCOL OUTLINE: Study randomized for Immunotherapy only. Randomize patients with no prior Chemotherapy to Arms III and IV, all others to Arms I and II.

Arm I: Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875.

Arm II: Single-agent Chemotherapy plus Immunotherapy. CACP plus Thymosin, no NSC number.

Arm III: 3-Drug Combination Chemotherapy. CACP; Bleomycin, BLEO, NSC-125066; Methotrexate, MTX, NSC-740.

Arm IV: 3-Drug Combination Chemotherapy plus Immunotherapy. CACP; BLEO; MTX; plus Thymosin.

STRATIFICATION BY: Participating institutions, performance status, previous radiotherapy or chemotherapy, immunological incompetence vs. competence.

SPECIAL STUDY PARAMETERS: Skin tests for recall antigens, T lymphocyte count, phytohemaglutinins, localized GVA in rats, bone marrow examination, IVP or renal scan, urine LDH, audiogram.

END POINTS: Objective tumor response, response/remission rate, duration of remission, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CACP - 100 mg/sqm/day iv on a 4-hour infusion with hydration and mannitol diuresis. Repeat course q 3 weeks.

Arm II: CACP as in Arm I plus Thymosin - 40 mg/sqm sc on alternating limbs on days 7, 12 and 17.

Arm III: MTX - 30 mg/sqm iv on days 1, 8 and 15 (because of toxicity, MTX was discontinued for all patients on day 8, continued for only source patients on day 15, report of June 1979); CACP - as in Arm I on day 2; BLEO - 30 mg iv on day 2 of first course, then q week for 6 doses (180 mg total dose). Repeat course q 3 weeks.

Arm IV: MTX; BLEO; CACP as in Arm III plus Thymosin as in Arm II.

Repeat course every 3 weeks for a minimum of 2 courses. Then continue therapy q 4 weeks indefinitely as long as there is evidence of tumor regression after 2 courses. Remove patients with progression or renal toxicity after 2 courses from study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: CACP - 10 mg vials; BLEO - 15 mg vials; MTX - 5 and 50 mg vials; Thymosin Fraction V - form not given.

DATE SUMMARIZED: 08/78

PATIENT ACCRUAL: 00290679

15.0028 CHEMOTHERAPY WITH FAC (5-FU/ADR/CTX) FOR METASTATIC CARCINOID TUMORS

Legha, S. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-253; MDA-DT-7763

OBJECTIVES:

I. Determine the efficacy in terms of response rate and effects on survival of chemotherapy with FAC: 5-fluorouracil (5-FU), adriamycin (ADR) and cyclophosphamide (CTX) in metastatic carcinoid tumors.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed measurable, metastatic carcinoid tumors or uncontrollable symptoms of carcinoid syndrome. Patients must not have had significant prior therapy with any drugs used in this study.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. FAC: 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271. When ADR has been administered to the maximum cumulative dose, substitute: Methotrexate, MTX, NSC-740.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, objective tumor response, survival time.

CURRENT STATUS: About 25 patients will be entered in 3-5 years.

DOSAGE SCHEDULE:

FAC: 5-FU - 300 mg/sqm iv on days 1 through 5; ADR - 50 mg/sqm iv on day 1 (maximum cumulative dose 450 mg/sqm); CTX - 400 mg/sqm on day 1. When the maximum ADR dose has been given, substitute: MTX - 40 mg/sqm iv or im on day 1. Repeat cycle q 21 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/78

15.0029 COMBINATION CHEMOTHERAPY WITH MTX/HC/ARA-C/CF AND RADIOTHERAPY FOR ADULT MENINGEAL LEUKEMIA OR LYMPHOMA

Stewart, D. J., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-266; MDA-DT-7813

OBJECTIVES:

I. Evaluate multiple drug intrathecal therapy with methotrexate (MTX)/hydracortisone (HC)/cytosine arabinoside (ARA-C) via Ommaya reservoir, and cranial irradiation as treatment for established meningeal leukemia and lymphoma.

II. Evaluate 'systemic reintensification' of chemotherapy as a method of preventing bone marrow relapse following primary CNS relapse.

III. Assess the frequency of long-term neurological sequelae in patients treated with the above regimens.

PROTOCOL ENTRY CRITERIA: Adult patients with established meningeal leukemia, including CML blast crisis, and lymphoma, including Burkitts. All patients must have an Ommaya reservoir.

PROTOCOL OUTLINE: Randomized study for reintensification only.

Induction: 3-Drug Combination Chemotherapy plus Hormone Therapy. Methotrexate, MTX, NSC-740; Cytosine Arabinoside, ARA-C, NSC-63878; Citrovorum Factor, CF, NSC-3590; plus Hydrocortisone, HC, NSC-10483.

Maintenance: 3-Drug Combination Chemotherapy plus Hormone Therapy plus Radiotherapy. MTX; HC; ARA-C; CF; plus 6 MeV Radiotherapy for patients previously untreated by Radiotherapy. Randomize patients to Reintensification Arm I or II.

Reintensification:

Arm I: No treatment.

Arm II: 3-Drug Combination Chemotherapy plus Hormone Therapy. MTX; HC; ARA-C; CF.

STRATIFICATION BY: Prior radiotherapy.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: About 15 patients will be entered per year.

DOSAGE SCHEDULE:

Induction: MTX - 20 mg intrathecal (it) or intraventricular (iven) on day 1 and q 7 days, followed 2 hours later by CF - 24 mg im or po given q 6 hours for a total of 4 divided (6 mg) doses; HC - 20 mg it or iven on day 1 and q 7 days; ARA-C - 100 mg (route not given) on day 3 and q 7th day. Repeat therapy for one course beyond CNS normalization, then enter patients to Maintenance.

Maintenance: MTX, CF, HC as in Induction on days 1, 15 and 29; ARA-C as in Induction on days 8, 22 and 36. Then MTX, CF, HC as in Induction on day 1; ARA-C as in Induction on day 2. Repeat q 4 weeks for 6 courses, then q 8 weeks until the end of the second year of CNS remission. Radiotherapy - give all patients with no prior Radiotherapy 3000 rad to whole brain and 3000 to involved spinal cord plus 1000 rad to the remainder of the cord.

Reintensification: Randomize patients following Radiotherapy.

Arm I: No Reintensification.

Arm II: MTX, CF, HC, ARA-C, dosage as in Induction, with MTX, CF and HC alternating with ARA-C q 3 days for 3 weeks, repeat q 6 months.

After 6 months decrease Maintenance to 1 course, as in Induction, given q 8 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

15.0030 COMBINATION CHEMOTHERAPY WITH CYVADIC (CTX/VCR/ADR/DTIC) FOR UNDIFFERENTIATED MALIGNANT NEOPLASMS

Bedikian, A. Y., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-268; MDA-DT-7812

OBJECTIVES:

I. Evaluate the efficacy of chemotherapy with CYVADIC: cyclophosphamide (CTX)/vincristine (VCR)/adriamycin (ADR)/imidazole carboxamide (DTIC) in the treatment of patients with undifferentiated malignant neoplasms.

PROTOCOL ENTRY CRITERIA: Adult patients with measurable undifferentiated malignant neoplasms. Patients must have adequate hematologic, hepatic, renal and cardiac functions and have had no previous therapy with the study agents. Patients must be without residual toxicity from any other therapy, which must have been terminated 3 weeks before.

PROTOCOL OUTLINE: Nonrandomized study.

4-Drug Combination Chemotherapy. Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Cyclophosphamide, CTX, NSC-26271; DTIC, NSC-45388; plus Actinomycin-D, ACT-D, NSC-3053, replacing ADR.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, objective tumor response.

CURRENT STATUS: 60 patients will be entered in 1 year.

DOSAGE SCHEDULE:

VCR - 1.5 mg/sqm (maximum dose 2 mg) iv on day 1 q 7 days for first 2 courses then on day 1 only of q 21-day course; ADR - 50 mg/sqm (40 mg/sqm for patients with inadequate marrow; maximum cumulative dose 500 mg/sqm) iv on day 2; CTX - 500 mg/sqm (200 mg/sqm for patients with elevated bilirubin levels or inadequate marrow) iv on day 2; DTIC - 250 mg/sqm (200 mg/sqm for patients with elevated bilirubin levels or inadequate marrow) on days 1 through 5. Give ACT-D to replace ADR when maximum dose is reached. Repeat course q 21 days or as soon as patient has recovered from hematologic toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

15.0031 CHEMOTHERAPY WITH AIM (L-ASP/MTX/IPP) FOR REFRACTORY ACUTE LYMPHOBLASTIC AND UNDIFFERENTIATED LEUKEMIA AND MALIGNANT LYMPHOMA

Yap, B. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-280; MDA-DT-7828

OBJECTIVES:

I. Determine the efficacy of combination chemotherapy with l-asparaginase (L-ASP), methotrexate (MTX), and ifosfamide (IPP) in patients with refractory acute lymphoblastic and acute undifferentiated leukemia.

II. Determine the qualitative and quantitative toxicity of this combination.

PROTOCOL ENTRY CRITERIA: Patients with acute lymphoblastic leukemia, acute undifferentiated leukemia or malignant lymphoma who have failed on primary therapy. Patients not refractory to prior therapy with MTX, L-ASP, or IPP or patients refractory to cyclophosphamide therapy are eligible. Patients must have normal serum creatinine and be off all previous chemotherapy for at least two weeks.

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. AIM: L-Asparaginase, L-ASP, NSC-109229; Ifosfamide, IPP, NSC-109724; Methotrexate, MTX, NSC-740.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, toxicity/morbidity of treatment.

CURRENT STATUS: 25 patients will be entered.

DOSAGE SCHEDULE:

AIM: MTX - 50 mg/sqm iv on day 1, 120 mg/sqm on day 10, 160 mg/sqm on day 20, 200 mg/sqm on day 30 and q 10 days thereafter; L-ASP - 20,000 IU/sqm iv on day 1 three hours following MTX, and on day 11 and q 10 days thereafter; IPP - 1500 mg/sqm (route not given) on days 2 through 4 and q 20 days for 3 days. For patients with abnormal serum creatinine or creatinine clearance less than 60 cc/min, give reduced MTX after consulting study chairman.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/79

15.0032 CHEMOTHERAPY WITH ICRF-159 AND CYTOSINE ARABINOSIDE FOR ACUTE LYMPHOCYTIC AND MYELOGENOUS LEUKEMIAS AND MALIGNANT LYMPHOMA

Frankel, L. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-281; MDA-P-7806

OBJECTIVES:

I. Investigate the therapeutic effectiveness of ICRF-159 and cytosine arabinoside in combination for induction and/or maintenance of acute leukemia and lymphoma after the 2nd or subsequent relapse.

II. Establish a dosage and administration schedule of these agents in combination to provide maximal effectiveness and the least combined toxicity.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven acute lymphocytic (ALL) or acute myelogenous (AML) or non-Hodgkin's lymphoma with marrow involvement who are resistant to standard forms of therapy and not eligible for higher priority protocols. Patients must have an M3 marrow with more than 25% blasts, a life expectancy of at least 6 weeks and have at least 2 weeks to recover from toxicity of prior therapy.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. ICRF-159, NSC-129943; Cytosine arabinoide, ARA-C, NSC-63878.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, remission duration, toxicity/morbidity of treatment.

CURRENT STATUS: 50 patients to be entered, about 10 to 12 per year.

DOSAGE SCHEDULE:

Induction: ICRF-159 - 15 mg/kg/day po in 3 or 4 divided doses on days 3 through 6; ARA-C - 90 mg/sqm/day iv on days 1 through 4. Repeat course on days 15 through 20. Increase dosage gradually in succeeding patients to ICRF-159 - 30 mg; ARA-C - 120 mg if toxicity is tolerable.

Maintenance: Enter patients in remission induced by ICRF-159/ARA-C or other agents. ICRF-159; ARA-C - as for Induction.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/78

15.0033 5-FU AND THYMIDINE VS 5-FU ALONE FOR ADENOCARCINOMAS OF THE BREAST, LUNG, OR COLORECTUM AND FOR MALIGNANT MELANOMAS

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PROTOCOL NUMBER(S) MDAR-297; MDA-DT-7844

OBJECTIVES:

I. Evaluate and compare the efficacy and toxicity of 5-fluorouracil (5-FU) alone and of 5-FU combined with thymidine (TdR) in the same patients with adenocarcinoma of the breast, lung, colorectum and malignant melanoma.

II. Establish correlations between clinical response, toxicities and changes in the pharmacologic and biochemical fate of 5-FU when given alone or in combination with TdR.

PROTOCOL ENTRY CRITERIA: Patients 15 to 70 years of age with histologically proven and objectively measurable adenocarcinoma of the breast, lung, colorectum or with malignant melanoma, not previously treated with 5-FU. Patients must have adequate bone marrow, liver and renal function unless the therapy is a life-saving measure. Patients must be off all prior chemotherapy or radiation therapy for four weeks and must not be eligible for higher priority therapy.

PROTOCOL OUTLINE: Randomized study.

Arm I: Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 2-Drug Combination Chemotherapy. 5-FU; Thymidine, TdR, NSC-21548.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, disease-free interval, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: At least 60 patients will be entered.

DOSAGE SCHEDULE:

Arm I: 5-FU - 500 mg/sqm/day (400 mg for poor-risk patients) iv for 5 days q 4 weeks.

Arm II: 5-FU - 250 mg/sqm (200 mg/sqm for poor-risk patients) iv on day 1; TdR - 15 grams iv.

Repeat course q 4 weeks. Evaluate patients after 2 courses. Cross over nonresponders to alternate therapy for two courses. Re-evaluate and continue treatment arm which yields better response and lower toxicity for a total period of two years or for one year after achieving remission. Remove from study patients with disease progression on both treatment arms.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/79

15.0034 CHEMOTHERAPY WITH FTORAFUR WITH AND WITHOUT ADR/CTX/CACP FOR METASTATIC ADENOCARCINOMA OF UNKNOWN PRIMARY ORIGIN

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PROTOCOL NUMBER(S) MDAR-334; MDA-DT-7917

OBJECTIVES:

I. Determine the efficacy of adriamycin/ftorafur in the treatment of patients with adenocarcinoma of unknown primary.

II. Determine the qualitative and quantitative toxicities of this combination.

Objectives I and II replaced by III, IV, and V (Revision, January 1980).

III. Determine the efficacy of ftorafur administered by the oral route in the treatment of patients with adenocarcinoma of unknown primary.

IV. Determine the efficacy of cyclophosphamide, adriamycin, cis-platinum (CAP) combination chemotherapy in the treatment of patients with adenocarcinoma of unknown primary refractory to ftorafur.

V. Study the pharmacology and determine the qualitative and quantitative toxicities of ftorafur administered by mouth.

PROTOCOL ENTRY CRITERIA: Patients with measurable, histologically proven, metastatic adenocarcinoma of unknown primary origin. Patients must have a minimum life expectancy of 12 weeks and must not have had prior chemotherapy. Patients must have adequate bone marrow, hepatic and renal function. Prior therapy must have terminated 4 weeks prior to entry, with recovery from toxicities.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: 2-Drug Combination Chemotherapy. Adriamycin, ADR, NSC-123127; Ftorafur, FT, NSC-148958. (Replaced by Regimen B. Revision, January 1980.)

Regimen B: Single-agent Chemotherapy. FT. Those with stable disease or tumor progression then receive 3-Drug Combination Chemotherapy. CAP: Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-119875.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: None.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response.

CURRENT STATUS: 45 patients will be entered.

DOSAGE SCHEDULE:

Regimen A: ADR - 60 mg/sqm (vary from 40 to 80 mg/sqm according to bilirubin values) iv on day 1; FT - 500 mg/sqm (increasing by 250 mg increments to 1000 mg/sqm if toxicity permits) po on days 1 through 10. Repeat course q 3 weeks as toxicity permits. Increase doses after 2 courses after recovery from myelosuppression. When FT dose reaches 1000 mg/sqm without toxicity, increase administration from 10 to 15 to 20 days per course. (Replaced by Regimen B. Revision, January 1980.)

Regimen B: FT - 500 mg/sqm po days 1 to 21 for 2 courses, escalating to 750, 1000, and 1500 mg/sqm/day for 21 days in absence of dose-limiting toxicity. Responders continue to receive FT for duration of response. Patients with SD receive a second course, following which those with PR continue FT and those with SD or DP are given CAP: CTX - 500 mg/sqm iv on day 1; ADR - 50 mg/sqm iv on day 1; and CACP - 12 mg/sqm/day iv for 4 days. The combination is given at 21-day intervals, recovery from toxicity permitting.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 04/80

15.0035 PHASE I-II STUDY OF HIGH-DOSE ASCORBIC ACID POTENTIATION OF ALKYLATING AGENTS IN CHILDREN WITH ADVANCED CANCER

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PROTOCOL NUMBER(S) MDAR-346; MDA-P-7901n

OBJECTIVES:

I. Determine the tolerance of ascorbic acid with an alkylating agent in children with cancer.

II. Determine the toxicity of high doses of ascorbic acid with alkylating agents cyclophosphamide and nitrogen mustard.

III. Evaluate the effectiveness of such combination therapies.

PROTOCOL ENTRY CRITERIA: Children with advanced cancer, including solid tumors and hematologic malignancies, who are in relapse and not eligible for higher priority treatment. Patients must have a life expectancy of 12 weeks or more, must have adequate liver and reasonable renal function, must have concluded any prior therapy 2 weeks prior to study entry and have recovered from its toxic effects.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients to Regimen A or B according to known drug resistance and suitability for their specific tumor.

Regimen A: Single-agent Chemotherapy plus Vitamin Therapy. Cyclophosphamide, CTX, NSC-26271; plus Ascorbic acid, VIT-C, NSC-33832.

Regimen B: Single-agent Chemotherapy plus Vitamin Therapy. Nitrogen Mustard, NM, NSC-762; plus VIT-C.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Response/remission rate, toxicity/morbidity of treatment, objective tumor response, survival.

CURRENT STATUS: 22 patients will be entered in about 4 years.

DOSAGE SCHEDULE: Enter all patients to Regimen A, then enter patients unresponsive to CTX to Regimen C, patients unresponsive to NM to Regimen B.

Regimen A: VIT-C - 6 mg/sqm/day continuous iv on days 1 through 9; plus CTX - 1200 mg/sqm iv single dose on day 7.

Regimen B: VIT-C - as in Regimen A; plus NM - 6 mg/sqm iv single dose on day 7.

Give a minimum of 2 courses of Regimen A or B.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/79

15.0036 SINGLE-AGENT CHEMOTHERAPY WITH DIBROMODULCITOL IN PATIENTS WITH ESOPHAGEAL CARCINOMA AND HEAD AND NECK CANCER

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PROTOCOL NUMBER(S) MDAR-365; MDA-DT-7955

OBJECTIVES:

I. Document the activity of dibromodulcitol (DBD) in patients with esophageal carcinoma and cancer of the head and neck.

PROTOCOL ENTRY CRITERIA: Patients with esophageal carcinoma and head and neck cancers who are ineligible for higher priority protocols. Patients may not have received prior chemotherapy but may have received prior surgery or radiotherapy. They must have measurable lesions, BUN less than 25 mg percent, serum creatinine less than 1.5 mg percent, and normal liver functions.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Dibromodulcitol, DBD, NSC-104800.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Liver and kidney function tests, blood counts, radiologic studies, esophagoscopy where applicable.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 25 patients will be entered into each group.

DOSAGE SCHEDULE:

DBD - 180 mg/sqm/day po for 10 days, repeated at 4-week intervals. A minimum of 2 courses shall be considered an adequate trial.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DBD - 50 mg tablets.

DATE SUMMARIZED: 02/80

15.0037 PHASE I-II IMMUNOTHERAPY WITH HUMAN IMMUNE INTERFERON FOR PATIENTS WITH DISSEMINATED CANCER

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PROTOCOL NUMBER(S) MDAR-374; MDA-DT-7992

OBJECTIVES:

I. Determine the pharmacological properties of human immune interferon.

II. Determine toxicity and biological effects of this preparation.

III. Determine the antitumor activity of this preparation in patients with malignant lymphoma, multiple myeloma, and breast cancer.

PROTOCOL ENTRY CRITERIA: Patients with metastatic breast cancer confined to lung and/or soft tissue regions with histological proof of malignancy, a minimal estimated life expectancy of 12 weeks, at least 50 percent estimated normal pulmonary function, and no more than 25 percent of pulmonary area on x-ray involved with tumor; those with previous history or evidence of severe hypertension, coronary artery disease, congestive cardiac failure, or major pulmonary dysfunction are eligible only with approval of principal investigator. Prior chemotherapy is not a requirement. Patients with well documented multiple myeloma and a life expectancy of 12 weeks; those previously untreated with chemotherapy are eligible. Patients with the following forms of lymphoma: Hodgkin's disease; nodular poorly differentiated lymphocytic lymphoma; well differentiated lymphocytic lymphoma; chronic lymphocytic leukemia; mixed histiocytic lymphocytic lymphoma. Patients with Hodgkin's disease and histiocytic lymphoma must have failed prior chemotherapy. Patients with nodular PDL, well differentiated lymphocytic lymphoma and mixed histiocytic lymphocytic lymphoma may be previously untreated.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Immunotherapy. Human Immune Interferon.

Regimen B: Immunotherapy. Human Immune Interferon plus Human Leucocyte Interferon.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Response/remission rate, duration of response, objective tumor response.

CURRENT STATUS: 15 patients with breast cancer, 15 with myeloma and 15 with malignant lymphoma will be entered.

DOSAGE SCHEDULE:

Regimen A: Pharmacological studies. Single injections (intramuscular) Immune Interferon in increasing doses. All patients are included in this Regimen, after which they will be entered in Regimen B.

Regimen B: Initial Phase II studies with small daily doses (3000 units) of human immune interferon plus regular dose of 3 million leucocyte interferon, by intramuscular route daily for minimal period of 56 days.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 05/80

15.0038 PHASE I-II CHEMOTHERAPY WITH VP-16213 FOR METASTATIC COLORECTAL CARCINOMA, OAT CELL CARCINOMA OF THE LUNG, AND HEPATOMA

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PROTOCOL NUMBER(S) MDAR-391; MDA-DT-8025

OBJECTIVES:

I. Determine the feasibility of hepatic arterial infusion of VP-16213 in the treatment of colorectal carcinoma with metastasis confined to the liver and of other regionally confined tumors such as hepatoma and oat cell carcinoma of the lung.

II. Determine the qualitative and quantitative toxicities of VP-16213 by hepatic arterial infusion.

III. Determine the response rate, response duration, and survival of patients treated by hepatic arterial infusion of VP-16213.

PROTOCOL ENTRY CRITERIA: Patients with colorectal carcinoma metastatic to the liver (without any evidence of extra-hepatic disease) or with other metastatic disease such as oat cell carcinoma of the lung where the bulk of the tumor is confined to the liver. Patients should have measurable disease and may have failed frontline therapy with floxuridine, mitomycin-C, and adriamycin by hepatic arterial infusion. Patients must have no chemotherapy for at least 3 weeks prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. VP-16213, VP-16, NSC-141540.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: CT scan, angiograph, CEA, radionuclide scanning, hematologic function test.

END POINTS: Response/remission rate, duration of response, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 20 patients will be entered.

DOSAGE SCHEDULE:

VP-16 - 100 mg/sqm by hepatic arterial infusion on days 1 through 3 q 3-4 weeks with increments of 25 mg/sqm depending on recovery from toxicity of previous cycle.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

15.0039 PHASE I-II HEPATIC ARTERIAL INFUSION OF DAVA FOR METASTATIC MELANOMA AND OTHER TUMORS CONFINED TO THE LIVER

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PROTOCOL NUMBER(S) MDAR-403; MDA-DT-8028

OBJECTIVES:

I. Determine the feasibility of continuous hepatic arterial infusion of vindesine given to patients with metastatic melanoma and other selected tumors regionally confined to the liver.

II. Determine response rate, duration of response, and survival of patients treated by hepatic arterial infusion of vindesine.

III. Compare the pharmacology of continuous intravenous infusion and continuous hepatic arterial infusion of vindesine.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven metastatic malignant melanoma confined to the liver and patients with breast cancer with metastatic disease primarily confined to the liver. Disease should be measurable. Patients must have a life expectancy of at least 12 weeks and have adequate bone marrow reserve. Patients must have been off chemotherapy and immunotherapy or radiotherapy for at least 4 weeks prior to entry and must have recovered from all toxic effects of previous therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Vindesine, DAVA, NSC-245467.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Angiography, radionuclide scan, ultrasound or CT scan of the liver; hematologic function tests.

END POINTS: Response rate, duration of response, objective tumor response.

CURRENT STATUS: About 20 evaluable patients will be entered.

DOSAGE SCHEDULE:

DAVA - 1 mg/sqm continuous hepatic arterial infusion over 24 hours daily for 5 days q 3 weeks; poor-risk patients (those with inadequate liver reserve) receive 0.75 mg/sqm.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

15.0040 CHEMOTHERAPY WITH VCR/CTX/ADR OR ACT-D/DTIC PLUS BCG IMMUNOTHERAPY AND VIRAL ONCOLYSATES FOR ADVANCED SARCOMA AND MELANOMA

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PROTOCOL NUMBER(S) MDAR-61

OBJECTIVES:

I. Determine the efficacy of combination chemoimmunotherapy with vincristine, cyclophosphamide, adriamycin and/or actinomycin-D, dimethyltriazeno imidazole carboxamide, scarified live Chicago Bacilli Calmette-Guerin and allogeneic or autologous tumor lysates ('viral oncolysates') for the maintenance of remission in two categories of solid tumors: sarcoma and melanoma in stratified groups of patients.

II. Compare Remission Induction and Maintenance thus obtained with that obtained previously by chemotherapy alone in large numbers of stratified groups of patients treated in the past three years within the Southwest Oncology Group and at the M.D. Anderson Hospital.

PROTOCOL ENTRY CRITERIA: Histologically confirmed metastatic or locally invasive soft tissue or bony sarcomas not amenable to further surgery or radiotherapy. Melanomas with poor prognosis: Clark's level III (inadequately excised head and neck or trunk lesions, and/or stage II disease, stage III disease with transit metastases or with positive lymph nodes after dissection, and melanomas with distant metastases.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with sarcoma to Regimen A; enter those with melanoma to Regimen B.

Induction and Maintenance:

Regimen A: 4-Drug Combination Chemotherapy plus Immunotherapy. Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; Adriamycin, ADR, NSC-123127. When maximum dose has been given, substitute Actinomycin D, ACT-D, NSC-3053; DTIC, NSC-45388. S cell lysate. BCG, live Chicago strain.

Regimen B: 4-Drug Combination Chemotherapy plus Immunotherapy. VCR, CTX, DTIC, ACT-D, and BCG as in Regimen A. Melanoma lysate.

STRATIFICATION BY: Type of tumor: melanoma or sarcoma; bone-marrow status: adequate or inadequate.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Objective tumor response, response/remission rate, response duration.

CURRENT STATUS: 42-45 patients will be entered per year.

DOSAGE SCHEDULE:

Regimen A: VCR - 1.5 mg/sqm (maximal single dose 2 mg) iv on day 1. CTX - 500 mg/sqm iv on day 2. ADR - 50 mg/sqm iv on day 2. When maximal total dose of 500 mg/sqm has been given, substitute ACT-D - 0.2 mg/sqm iv on days 3, 4, and 5 for the first course, then, if tolerated, 0.2 mg/sqm iv on days 1 through 5. Maximal total dose per course, 2.5 mg. DTIC - 250 mg/sqm iv on days 1 through 5. Repeat Chemotherapy q 28 days. On days 17 and 24 in between courses of Chemotherapy give Immunotherapy: S cell lysate - contents of 1 vial applied ic to 2 or 3 sites. BCG - contents of 1 ampule by scarification into the skin over and around the areas of lysate application. Repeat Immunotherapy twice a month for 10 courses, then give Immunotherapy once a month for 14 additional courses.

Regimen B: Give VCR, CTX and DTIC as in Regimen A; plus Act-D - 0.2 mg/sqm/day iv on days 1 through 5 of each course. Immunotherapy: BCG and viral oncolysate as in Regimen A, substituting Melanoma lysate for S cell lysate.

Give a total of 24 courses of multimodal therapy, Regimen A or Regimen B, over 2 years.

Dosage modifications for patients with inadequate bone-marrow reserves and for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 03/76

15.0041 IMMUNOTHERAPY WITH BCG OR MER-BCG FOR CUTANEOUS METASTASES OF CANCER

Pinsky, C. M., (212-794-7595) Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York, 10021, United States of America

PROTOCOL NUMBER(S) MSKCC-7010

OBJECTIVES:

I. Determine whether the injection of BCG or MER-BCG into the tumor produces regression of injected and non-injected tumor nodules.

PROTOCOL ENTRY CRITERIA: Patients with cutaneous metastases of cancer.

PROTOCOL OUTLINE: Nonrandomized study. For each patient, a number of lesions are treated and a number are left untreated to act as controls.

Immunotherapy. BCG-Lilly, BCG, no NSC number; or MER-BCG, MER, NSC-143769.

STRATIFICATION BY: None.

SPECIAL STUDY PARAMETERS: Skin tests for delayed hypersensitivity; in vitro immune parameters of lymphocyte, granulocyte, and macrophage function.

END POINTS: Regression of injected tumors, regression of non-injected tumors, recurrence rate, survival.

CURRENT STATUS: 93 patients have been entered.

DOSAGE SCHEDULE:

BCG - average dose is approximately 10 to the 7th organisms intralesionally (schedule not given); or MER - 0.1 to 0.5 mg (depending on the size of the lesion) injected intralesionally at each metastatic site (schedule not given). Treatment continues until progressive disease or toxicity (hypersensitivity reactions, chills, fever, malaise, headache) develops.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by the investigator.

DATE SUMMARIZED: 12/80

15.0042 IMMUNOTHERAPY BY INFUSION OF ALLOGENIC LYMPHOCYTES IN PATIENTS WITH ADVANCED CARCINOMA

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PROTOCOL NUMBER(S) MSKCC-743

OBJECTIVES:

I. Assess whether infusion of ABO compatible but otherwise randomly selected allogenic lymphocytes will produce a favorable therapeutic effect in patients with advanced cancer.

II. Assess whether this therapy will alter response in specific immune test systems, even if the disease itself is not favorably altered.

PROTOCOL ENTRY CRITERIA: Patients with advanced cancer who have failed on conventional and Phase II drug therapy.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy. Infusion of allogenic lymphocytes.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Immunobiology profile.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, objective tumor response, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Administer iv injection of 10 to the 10th leucocytes from ABO blood type, cross-matched, leucoagglutinin-compatible, SH antigen negative, but otherwise random donor at varying intervals from q 7 to q 14 days for a total of 8 to 15 infusions. Where feasible, mis-match donor-recipient pairs by sex to facilitate detection of chimeric development.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 11/77

15.0043 L-10M CHEMO/ENDOTHERAPY FOR ADULT ACUTE LYMPHOBLASTIC LEUKEMIA AND NULL CELL OR T CELL LYMPHOBLASTIC LYMPHOMA

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PROTOCOL NUMBER(S) MSKCC-7761; MSKCC-L-10M

OBJECTIVES:

I. Improve the L-10 Protocol by modifications to include combined doses of adriamycin and cytoxan at the end of Induction, and intravenous infusions of cytosine arabinoside to be given with methotrexate during Consolidation, in an effort to prevent early relapses noted in some patients on L-10.

PROTOCOL ENTRY CRITERIA: Adult patients 15 years or older with acute lymphoblastic leukemia, or null cell or T cell lymphoblastic lymphoma, previously untreated or treated with minimal chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Induction:

4-Drug Combination Chemotherapy plus Hormone Therapy. Vincristine, VCR, NSC-67574; Adriamycin, ADR, NSC-123127; Methotrexate, MTX, NSC-740; Cyclophosphamide (Cytoxan), CTX, NSC-26271; plus Prednisone, PRED, NSC-10023.

Consolidation:

5-Drug Combination Chemotherapy plus Radiotherapy. Cytosine arabinoside, ARA-C, NSC-63878; MTX; 6-Thioguanine, TG, NSC-752; L-Asparaginase, L-ASP, NSC-106977; CTX. (Therapy with VCR, PRED, and randomization to Pseudomonas vaccine added in May 1978.)

Maintenance:

First sequence. 5-Drug Combination Chemotherapy plus Hormone Therapy. VCR; ADR; 6-Mercaptopurine, 6-MP, NSC-755; MTX; Actinomycin-D (Dactinomycin), ACT-D, NSC-3053; plus PRED.

Second sequence. 6-Drug Combination Chemotherapy plus Hormone Therapy. VCR; BCNU, BCNU, NSC-409962; CTX; 6-MP; MTX; ACT-D; plus PRED.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: CTT scan, pneumoencephalogram.

END POINTS: Response/remission rate, disease-free interval, recurrence rate, length of survival.

CURRENT STATUS: 28 patients have been entered as of September 1980; 60 patients will be entered within 3 to 4 years.

DOSAGE SCHEDULE:

Induction:

VCR - 1.5 to 2.0 mg/sqm iv on days 0, 7, 14, 21 and 28; PRED - 60 mg/sqm po in 3 divided doses daily from day 0 to day 36 and tapered over next 7 days; ADR - 20 mg/sqm iv on days 16, 17 and 18, and 30 mg/sqm iv push on day 33; MTX - 6 mg/sqm it on days 2, 4, 13, 15, 31 and 33; CTX - 600 mg/sqm iv push on day 33. On or about day 30, an Ommaya reservoir will be placed in the frontotemporal area of the skull if the presenting WBC exceeds 20,000/cumm and an M-1 marrow is achieved; if marrow is not M-1, the Ommaya is delayed until CTX and ADR are given (day 33). A rest period of 10 to 14 days follows Induction to permit bone marrow recovery.

Consolidation:

ARA-C - 200 mg/sqm iv infusion over 24 hours daily for 5 days starting on days 47, 82, and 117, and 300 mg/sqm po daily in 2 divided doses for 12 to 20 doses (until hypocellularity, depending on drug tolerance) starting on days 61, 96, and 131; MTX - 15 mg/sqm iv daily for 5 days starting on days 47, 82, and 117; TG - 240 mg/sqm po in 2 divided doses daily for 12 to 20 doses (until hypocellularity) starting on days 61, 96, and 131.

Intrathecal MTX - if initial WBC is less than 20,000 cumm and an Ommaya reservoir is not in place, 6 mg/sqm is given daily on days 47, 82, and 117 and twice daily qod on days 61, 63, 96, 98, 113, and 115. If WBC is greater than 20,000/cumm and Ommaya reservoir is in place, MTX - 6 mg/sqm is given on the same schedule by the Ommaya reservoir. The BUN must be lower than 20 mg percent.

L-ASP - 60,000 I.U./sqm tiw for 6 doses starting on day 140 if skin test for L-ASP sensitivity is negative; if test is positive, desensitization of patient must occur before administering L-ASP. CTX - 1200 mg/sqm (1000 mg/sqm for patients over 60 years of age) iv on day 154. A rest period of 2 weeks follows CTX therapy to allow bone marrow recovery. Radiotherapy will be administered to patients with lymphoblastic lymphoma with bulky tumor areas (larger than 5 cm) or patients with ALL with bulky mediastinal or other massive nodal involvement. RT is to begin immediately following recovery from L-ASP and CTX and may continue into Maintenance therapy. Doses and schedules for RT will depend upon initial bulky disease, patient's hematologic status, and evidence of tumor progression during protocol.

Consolidation modified as of May 1978 as follows:

Patients will receive the alternating cycles of ARA-C with MTX and ARA-C with TG as per the original protocol. In addition, just prior to the beginning of the fourth phase, on demonstration of rising blood counts, the patients will receive VCR - 1.4 mg/sqm iv (maximum 2 mg) with PRED - 60 mg/sqm po in 3 divided doses daily for 7 days and VCR - 1.4 mg/sqm iv (maximum 2 mg) on day 8. After a rest of 2-3 days, patients are hospitalized and receive ARA-C and TG q 12 hours as prescribed in the original protocol. All other elements in the original protocol remain unchanged. For patients who have relapsed either on the original L-10 protocol or on the L-10M protocol, reinduction therapy remains the same. Consolidation, however, is shortened; treatment with L-ASP begins immediately upon completion of the third cycle. Following treatment with L-ASP, a bolus of CTX is administered. In 10-14 days, the eradication phase of treatment as described in the original protocol begins. All previously untreated patients with acute lymphoblastic leukemia are randomized for pseudomonas vaccine, given during the eradication phase only, prior to VCR-PRED, prior to 6MP-MTX, and prior to ACT-D. All patients on the L-10M protocol are randomized for the vaccine.

Maintenance:

First sequence. VCR - 2 mg/sqm iv on days 0 and 7; PRED - 180 mg/sqm po in 2 divided doses daily on days 0 through 7 beginning 8 to 12 hours after initial VCR dose, stopping abruptly on day 8; ADR - 20 mg/sqm iv for 3 consecutive days beginning on day 14. Rest period of 2 weeks. 6-MP - 90 mg/sqm po daily for 30 days; MTX - 20 mg/sqm po q 5 to 7 days for 4 to 5 doses beginning 3 days after initial dose of 6-MP, and 6.25 mg/sqm it on first and third day of 6-MP/MTX cycle in patients with platelet count greater than 50, 000/cumm. ACT-D - 1000 gamma/sqm iv as single dose given 7 days after conclusion of 6-MP/MTX therapy. Rest period of 7 days.

Second sequence. VCR/PRED as in first sequence. BCNU - 80 mg/sqm iv as single dose with CTX - 800 mg/sqm iv as single dose on day 14. Rest period of 2 weeks. 6-MP, MTX (po, it), ACT-D as in first sequence. At conclusion of second sequence, repeat complete Maintenance program and continue rotation for one year.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/80

15.0044 PILOT PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED SOLID TUMORS AND MALIGNANT LYMPHOMAS

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PROTOCOL NUMBER(S) MSKCC-7918

OBJECTIVES:

I. Evaluate the antitumor activity of AMSA in the treatment of a broad range of human malignancies.

PROTOCOL ENTRY CRITERIA: Patients 75 years old or less with measurable, histologically confirmed malignancy not curable by surgery or radiotherapy. Disease types included are: lung, colorectal, breast and ovarian carcinoma as well as malignant melanoma or lymphoma. Patients must have adequate hematologic, hepatic, and renal function. Patients must have a performance status of [illegible] or more and a minimum life expectancy of 2 months, and may not be eligible for conventional therapy. Patients must have had no recent radiotherapy to primary or metastatic disease (except to brain) and no recent chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. AMSA, NSC-249992.

STRATIFICATION: None.

SPECIAL STUDY PARAMETERS: Liver, bone and brain scans, CEA, 5-prime nucleotidase.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment, survival time.

CURRENT STATUS: 30 to 40 patients will be entered if a major response is observed.

DOSAGE SCHEDULE:

AMSA - 120 mg/sqm (90 mg/sqm for patients with a performance status of 50 to 70 or evidence or suspicion of compromised marrow) iv on day 1. Repeat q 3 weeks, or when hematologic toxicity permits. Continue therapy for all patients until disease progression or unsatisfactory stable disease of at least 3 months duration.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 11/79

15.0045 CRANIAL VAULT RADIOTHERAPY PLUS INTRATHECAL MTX WITH OR WITHOUT IT THIOTEPA FOR MENINGEAL CARCINOMATOSIS

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PROTOCOL NUMBER(S) NCI-76-C-63; NCI-MB-80

OBJECTIVES:

I. Determine whether the addition of intrathecal thiotepa to the standard regimen of craniospinal radiotherapy, intrathecal methotrexate, and dexamethasone improves the survival of patients with meningeal carcinomatosis arising from breast cancer, melanoma, leukemia, or lymphoma.

II. Evaluate patient tolerance to these regimens.

III. Assess the effect of coexisting CNS mass lesions on response and survival.

IV. Evaluate the relationship of CSF methotrexate levels to neurotoxicity.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented breast cancer, melanoma, lymphoma, or leukemia who have meningeal carcinomatosis diagnosed by the presence of malignant cells in the CSF. Patients must be under the age of 65 and must have a creatinine of less than 2.5 mg percent. They may not have received prior radiotherapy to the cranial vault, and there must be no evidence of CSF infection.

PROTOCOL OUTLINE: Enter all patients on Regimen A. Patients with breast cancer and lymphoma will subsequently be randomized to Arms I and II; all others will enter Arm II.

Regimen A. Radiotherapy. Linear accelerator equipment.

Arm I: Single-agent Chemotherapy plus Hormone Therapy. Methotrexate, MTX, NSC-740; Dexamethasone, DM, NSC-34521.

Arm II: 2-Drug Combination Chemotherapy plus Hormone Therapy. MTX; Thiotepa, NSC-6396; DM.

STRATIFICATION BY: Coexisting cranial CNS mass lesions (yes vs. no), disease (breast cancer vs. lymphoma vs. melanoma).

SPECIAL STUDY PARAMETERS: Hemogram, kidney function tests, electrolytes, skull x-rays, brain scan, EEG, EMI, CSF studies.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: 15-20 patients will be entered in 2-3 years.

DOSAGE SCHEDULE:

Regimen A: 3000 rads whole brain irradiation over 2 weeks by opposing bilateral portals in 5 weekly fractions of 300 rads each. No prophylactic spinal therapy. Intradural lumbar spinal canal disease should receive 3000 rads in 300-rad fractions, 5 fractions per week. Thoracic or cervical cord lesions should receive 2700 rads in 9 fractions.

Arm I: MTX - 12 mg it q 4 days until all malignant cells have disappeared from the CSF; thereafter, 12 mg it q other week for 4 doses, then monthly; DM - 3 mg/sqm po at the time of MTX administration and at hours 12, 24, 36, and 48, then daily. After the initial 1-month Induction, attempt to taper DM dose to zero.

Arm II: MTX - 12 mg it; Thiotepa - 10 mg it 48 hours after MTX. Repeat weekly until all malignant cells have disappeared from the CSF, then q 2 weeks for 4 courses, then monthly. DM - as in Arm I.

Chemotherapy may be given concurrently with Radiotherapy. Give at least 4 cycles before declaring failure. Treat all patients until progressive disease is demonstrated. Patients who have a good initial response but relapse on the monthly maintenance part of the protocol should have reinduction attempted before being declared failures.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

15.0046 PROSPECTIVE RANDOMIZED TRIAL OF HLA-MATCHED PLATELET TRANSFUSIONS AS SUPPORTIVE THERAPY IN THROMBOCYTOPENIC CANCER PATIENTS

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PROTOCOL NUMBER(S) NCI-77-C-181

OBJECTIVES:

I. Compare, in a prospective randomized trial, HLA-matched and HLA-mismatched platelet transfusions in thrombocytopenic cancer patients with regard to: number and frequency of transfusions required; mean increments in platelet counts after transfusion; frequency of transfusion reactions; number of bleeding episodes; development of anti-HLA antibodies; and length of time until patients become refractory to the treatment strategy (matched vs. mismatched).

II. Determine how often patients refractory to one strategy respond when crossed to the alternate strategy and what differences exist in the subsequent responses.

III. Determine whether the order of strategy results in a difference in the total length of time patients respond to platelet transfusions.

IV. Determine in patients refractory to both matched and mismatched platelet transfusions whether the type of platelets transfused results in a difference in: the number of transfusions required; the mean increments in platelet counts after transfusion; and the frequency and time to the development of significant bleeding episodes.

PROTOCOL ENTRY CRITERIA: Cancer patients whose platelet counts are not greater than 20,000, with or without bleeding, and those with platelet counts of greater than 20,000 in the face of invasive diagnostic or therapeutic procedures. Patients may not have received more than 5 blood component transfusions prior to entry. There must be an adequate number of HLA-matched donors for any given patient.

PROTOCOL OUTLINE: Randomized study.

Arm I: HLA-Matched Platelet Therapy.

Arm II: HLA-Mismatched Platelet Therapy.

STRATIFICATION BY: Cancer type, bone marrow involvement (yes vs. no).

SPECIAL STUDY PARAMETERS: Hematologic parameters, clotting studies, bone marrow examination, liver/spleen scan, ABO and HLA typing, serum anti-HLA antibodies, blood chemistries.

END POINTS: Number and frequency of platelet transfusions required, increments in platelet counts following transfusions, frequency of transfusion reactions, number of bleeding episodes, development of anti-HLA antibodies, length of time to refractoriness to platelet transfusion.

CURRENT STATUS: 53 patients will be entered on each arm over about 2 years.

DOSAGE SCHEDULE:

Arm I: Transfuse HLA-matched platelets as necessary for a platelet count of less than 20,000 or bleeding due to thrombocytopenia.

Arm II: Transfuse HLA-mismatched platelets as in Arm I.

When patients on either arm have an increment in the platelet count of less than 2.5 after 3 successive transfusions, cross to the alternate arm. When 3 consecutive transfusions on the alternate strategy result in an increment of less than 2.5, randomize to receive either matched or mismatched platelets. Patients go off study when bleeding becomes uncontrollable.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not applicable.

DATE SUMMARIZED: 01/81

15.0047 PHASE II IMMUNOTHERAPY WITH ANTI-THYMOCYTE GLOBULIN FOR MALIGNANT LYMPHOMA OR LEUKEMIA

Fisher, R. I., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-78-C-35; NCI-MB-100; NCI-VA-MOB-773

OBJECTIVES:

I. Evaluate the activity of anti-thymocyte globulin in patients with mycosis fungoides, Sezary syndrome, non-Hodgkin's lymphoma, Hodgkin's disease, or leukemia.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed mycosis fungoides, Sezary syndrome, non-Hodgkin's lymphoma, Hodgkin's disease, or leukemia. Patients with mycosis fungoides and Sezary syndrome must have failed prior electron beam radiotherapy and systemic chemotherapy, and patients with all other lymphomas or leukemia must have failed systemic chemotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Immunotherapy. Anti-thymocyte globulin, ATG.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hemogram, electrolytes, liver and kidney function tests, chest x-ray and KUB, recall skin tests, peripheral blood T and B cell counts.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: About 10 patients with Sezary syndrome or mycosis fungoides and 10 patients with malignant lymphoma or leukemia will be entered during a 2-year period.

DOSAGE SCHEDULE:

ATG - 15 mg/kg/day iv over 4-6 hours for 14 days. Patients responding to the 2-week trial will receive treatment for 7 days each month until progressive disease.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: ATG - 250 mg ampules.

DATE SUMMARIZED: 10/80

15.0048 PHASE II CHEMOTHERAPY WITH INTERMITTENT HIGH-DOSE CACP FOR LUNG CANCER AND OTHER TUMORS

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PROTOCOL NUMBER(S) NCI-78-C-60

OBJECTIVES:

I. Determine the response rate and duration of response in patients with lung cancer and other malignant tumors treated with high-dose cis-platinum.

II. Determine the toxicity of this therapy with hydration and diuresis.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented lung cancer and other malignancies no longer amenable to curative surgery or radiotherapy who have measurable or evaluable disease. Hematologic and renal function must be adequate. Patients must have an expected survival of at least 2 months and a Zubrod performance status of not more than 3. Patient age must not be greater than 75, and there may be no serious complicating medical condition.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. cis-Platinum, CACP, NSC-119875; Mannitol, NSC-9256.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Tumor measurement, hemogram, renal function studies, electrolytes, liver function tests, acid phosphatase, chest x-ray, appropriate scans, IVP (prostate cancer), upper GI series (gastric cancer), endoscopy (gastric cancer), bone marrow if abnormal, bronchoscopy (lung cancer), protein electrophoresis and quantitative immunoelectrophoresis, audiogram.

END POINTS: Response rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: 14-20 patients of each histologic type will be needed for statistical validity.

DOSAGE SCHEDULE:

CACP - 75 mg/sqm iv over 15-30 minutes following prehydration and concurrent mannitol diuresis q 3 weeks for a minimum of 2 doses in the first 3 patients to ascertain hematologic tolerance. In the absence of significant myelosuppression, start subsequent patients on 120 mg/sqm as the initial dose. Give small cell carcinoma patients 2 courses and all other patients 3 courses prior to restaging. Continue patients with stable disease and objective response until progression or unacceptable toxicity. Patients with progressive disease go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CACP - 10 mg vials.

DATE SUMMARIZED: 10/80

15.0049 PHASE II CHLOROZOTOCIN FOR CARCINOMA OF THE BREAST AND OVARY, MELANOMA, ISLET CELL CARCINOMA, LYMPHOMA, SARCOMA, AND OTHER TUMORS

Lippman, M. E., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-78-C-97; NCI-MB-8402

OBJECTIVES:

I. Assess the antitumor activity of chlorozotocin given as a single dose on a 6-week schedule in patients with advanced cancer of the breast and ovary, melanoma, islet cell carcinoma, lymphomas, sarcomas, and other malignancies.

II. Study the pharmacology of chlorozotocin in these patients.

PROTOCOL ENTRY CRITERIA: Patients with histologically documented measurable malignancy that is not amenable to conventional therapy, including carcinoma of the breast, malignant melanoma, islet cell carcinoma, malignant lymphoma, soft tissue sarcoma, osteogenic sarcoma, and ovarian carcinoma. Patients must have failed previous chemotherapy regimens, and must have recovered from any resultant severe toxicity. Patients must have at least minimal hematologic function, and liver and kidney function tests must be within normal limits. Patients must not be pregnant.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Chlorozotocin, CLZ, NSC-178248.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hemogram, renal function tests, chest x-ray, tumor measurements, circulating tumor markers if present, quantitative immunoglobulins, delayed hypersensitivity skin tests, A and B lymphocyte assays.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

CLZ - 90-120 mg/sqm iv q 6 weeks, depending on extent of prior Chemotherapy. In the absence of marrow toxicity after 2 cycles escalate by 30 mg/sqm q 2 cycles to a maximum of 150 mg/sqm. Continue treatment as long as there is evidence of response or stable disease. Patients with progressive disease after 2 cycles go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: CLZ - 50 mg vials.

DATE SUMMARIZED: 08/80

15.0050 PILOT STUDY OF WR-2721 FOR BONE MARROW PROTECTION IN PATIENTS WITH ADVANCED CANCER RECEIVING HEMIBODY IRRADIATION

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PROTOCOL NUMBER(S) NCI-79-C-105

OBJECTIVES:

I. Evaluate the efficacy of WR-2721 for protection of the bone marrow against radiation in advanced cancer patients undergoing hemibody radiotherapy.

II. Determine the dose of radiation for which a given dose of WR-2721 affords protection.

PROTOCOL ENTRY CRITERIA: Adult patients with advanced cancer who will receive palliative hemibody radiotherapy.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy with Radioprotective Therapy. 6 MeV linear accelerator. WR-2721, NSC-296961.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Blood pressure, hemogram, reticulocytes.

END POINTS: Hematologic toxicity, number of treatments tolerated, survival.

CURRENT STATUS: Nine patients will be entered.

DOSAGE SCHEDULE:

WR-2721 - 500 mg/sqm iv bolus 15 minutes prior to each Radiotherapy treatment. Radiotherapy - 800 rads over 4 weeks in 200-rad fractions, 1 fraction per week, through opposing ports. If thrombocytopenia and leukopenia do not require support after treatment of the first 2 patients, radiation dose will be escalated to 300 rads/fraction (total 1200 rads/4 weeks) in the next 2 patients, then to 400 rads/fraction (total 1600 rads/4 weeks) in the subsequent 5 patients.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: WR-2721 - 500 mg vials.

DATE SUMMARIZED: 08/80

15.0051 PHASE II CLINICAL TRIAL OF 13-CIS-RETINOIC ACID FOR ADVANCED BREAST CANCER AND OTHER SOLID TUMORS

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PROTOCOL NUMBER(S) NCI-79-C-119; NCI-MB-133

OBJECTIVES:

I. Determine the antitumor activity of 13-cis-retinoic acid in patients with advanced malignancies, including breast cancer, malignant melanoma, and carcinomas of the testis and ovary.

II. Define the toxicity of 13-cis-retinoic acid when administered orally as a single daily dose.

III. Study the pharmacokinetics of 13-cis-retinoic acid in humans.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven advanced malignancy that is not amenable to conventional therapeutic modalities. Included are carcinoma of the breast, malignant melanoma, testicular carcinoma, and ovarian carcinoma. Patients must have measurable disease. Patients may have received prior chemotherapy. Bone marrow function must be at least minimal, and liver and kidney function tests must be within normal limits. The Karnofsky performance status must be greater than 40 and the minimum expected survival 2 months.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. 13-cis-Retinoic acid, no NSC number.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hemogram, kidney and liver function tests, SMA-21, chest x-ray, tumor measurements, circulating tumor markers if present, bone scan, metastatic survey, liver scan, other scans as indicated to follow measurable disease.

END POINTS: Response/remission rate, duration of response, objective tumor response, survival, toxicity/morbidity of treatment

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

13-cis-Retinoic acid - escalating single daily oral doses as follows: 0.5 mg/kg on days 1-3; 1 mg/kg on days 4-7; 2, 3, and 4 mg/kg/day during weeks 2, 3, and 4, respectively; and 5 mg/kg/day during weeks 5 through 16. No treatment during weeks 16-20, then repeat cycle from day 1 of week 2. Continue treatment as long as there is a response or stable disease. Patients with progressive disease anytime after 4 weeks of therapy go off study.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 13-cis-Retinoic acid - 5, 10, 20, and 40 mg capsules.

DATE SUMMARIZED: 10/80

15.0052 INTRAVENOUS MISONIDAZOLE AS A RADIOSENSITIZER IN PATIENTS RECEIVING RADIOTHERAPY FOR ADVANCED CANCER

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PROTOCOL NUMBER(S) NCI-79-C-60

OBJECTIVES:

I. Evaluate the patient tolerance and toxicity of administering misonidazole iv 2 hours prior to radiation therapy in patients being treated for advanced cancer.

II. Study the pharmacokinetics of iv misonidazole.

PROTOCOL ENTRY CRITERIA: Patients with advanced malignancy with appropriate indications for radiotherapy. There must be no prior history of renal or hepatic disease, and tests of liver and kidney function should be within normal limits. There may be no preexisting neurological disorder, and the Karnofsky performance score must be greater than 40. There may be no treatment with nitroimidazole-type drugs within 2 weeks prior to treatment.

PROTOCOL OUTLINE: Nonrandomized study.

Radiotherapy with Radiosensitization. Misonidazole, MNI, NSC-261037.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Misonidazole levels in plasma, urine, and CSF (when indicated); neurologic monitoring.

END POINTS: Toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

MNI - 1.5 g/sqm iv over 5 minutes twice weekly 2 hours before radiation therapy, for a total of 10 doses. In the absence of Grade 3 neurotoxicity, escalate dose by 0.5 g/sqm in each cohort of 3 patients.

Dosage modifications for toxicity are given.

DOSAGE FORMS: MNI - 500 mg vials.

DATE SUMMARIZED: 10/80

15.0053 PHASE II AND PHARMACOLOGICAL STUDIES OF INTRAPERITONEAL 5-FU FOR STAGE III OVARIAN CARCINOMA AND SELECTED OTHER TUMORS

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PROTOCOL NUMBER(S) NCI-79-C-79; NCI-MB-CPB-127

OBJECTIVES:

I. Define the activity of intraperitoneal 5-fluorouracil (5-FU) in Stage III ovarian carcinoma and in selected other tumors confined to the abdomen.

II. Correlate peritoneal and plasma 5-FU levels with systemic toxicity and tumoricidal effect.

III. Correlate indocyanine green clearance to the presence or absence of hepatic disease ang 5-FU metabolism.

IV. Correlate systemic toxicity and plasma 5-FU levels with bone marrow FdUMP levels.

V. Correlate clinical response to 5-FU with response of cultured tumor cells from these patients to 5-FU in an in-vitro assay.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed Stage III ovarian carcinoma or metastatic carcinoma confined to intraperitoneal and hepatic sites, e.g., colon. Patients must have measurable disease. Patients with ovarian carcinoma must have failed standard chemotherapy. Patients may have had prior therapy with 5-FU. Bone marrow function must be adequate. Patients may not have extensive peritoneal adhesions.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Plasma and peritoneal fluid 5-FU levels, hemogram, electrolytes, chemistry panel.

END POINTS: Response/remission rate, duration of response, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: A minimum of 25 patients with ovarian cancer will be entered.

DOSAGE SCHEDULE:

5-FU - 1040 mg in 2 liters of dialysis solution instilled ip via a Tenckhoff silastic dialysis catheter for 2 hours. Repeat treatment q 2 weeks, escalating the 5-FU dose by 65 mg/2 liters each course until clinical toxicity is reached. If complete remission is reached, therapy will continue for 4 more courses before detailed restaging. All patients will be treated for a minimum of 2 instillations. If there is objective evidence of disease progression after that time, patients are declared failures and therapy is changed. For patients with intrahepatic metastases, peritoneoscopy and 6 liver biopsies will be performed. Patients in whom the only initial evidence of objective disease is obtained by peritoneoscopy will be treated until disease progression or for 6 cycles and then undergo repeat peritoneoscopy. Patients with negative peritoneoscopy will undergo laparotomy to determine pathologic remission if this is uncertain. Patients in CR will be followed off therapy by peritoneoscopy q 6 months for a year, then observed.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

15.0054 PHASE II STUDY OF HUMAN LYMPHOBLASTOID INTERFERON VS STABILIZED POLY I:C FOR ACUTE MYELOCYTIC LEUKEMIA, CLL, AND VARIOUS SOLID TUMORS

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PROTOCOL NUMBER(S) NCI-79-C-80; NCI-POB-7901; BCRP-7914

OBJECTIVES:

I. Determine the therapeutic efficacy of human lymphoblastoid interferon and stabilized poly I:C in patients with acute myelocytic leukemia who are in their first bone marrow relapse and have received no previous Induction for this relapse and in patients with various solid tumors in relapse.

PROTOCOL ENTRY CRITERIA: Adult patients with acute myelocytic leukemia who are in their first bone marrow relapse after having been treated with standard drugs but without treatment for the relapse. Patients with various solid tumors in relapse, including but not limited to small cell carcinoma of the lung, breast carcinoma, non-Hodgkin's lymphoma, CLL, melanoma, myeloma, sarcoma, and neuroblastoma. Solid tumor patients will have failed the entire sequence of higher priority therapies prior to entry on this study.

PROTOCOL OUTLINE: Randomized study. Until Interferon becomes available patients may be entered on Poly I:C nonrandomly.

Induction:

Arm I: Immunotherapy. Human Lymphoblastoid Interferon, Interferon.

Arm II: Immunotherapy. Stabilized Poly I:C, Poly IC, NSC-120949.

Patients with complete response, stable disease, or improved disease proceed to Maintenance with the Induction agent. Failures may be crossed over to the alternate arm.

Maintenance:

Arm III: Immunotherapy. Interferon.

Arm IV: Immunotherapy. Poly IC.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Hemogram, liver and kidney function tests, bone marrow aspiration, CSF examination, serum for interferon determination and immunological tests, serum protein electrophoresis, PT/PTT/TT, ANA, SGPT, LDH, CPK.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Between 90 and 150 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Interferon - 2.5 x 10 to the sixth reference units im on day 1; 10 to the seventh units in 2 divided doses on day 2 and daily thereafter for a total of 30 days.

Arm II: Poly IC - 12 mg/sqm iv infusion over 60 minutes q other day for 30 days.

Minimum treatment period is 1 month. For AML patients a second month of Induction therapy should be given if the marrow improves from M3 to M2 by day 30. For solid tumor patients whose disease is stable or improved by day 30, a second month of Induction therapy should be given. Patients with stable or improved disease at the end of 2 months should proceed to Maintenance with the Induction agent. Failures may be crossed over to the alternate Induction arm. CR proceed at once to Maintenance with same agent.

Arm III: Interferon - 5 x 10 to the sixth im 3 times weekly for 18 months.

Arm IV: Poly IC - 12 mg/sqm iv 3 times weekly for 18 months.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 08/80

15.0055 PHASE II EVALUATION OF CHEMOTHERAPY WITH AD-32 FOR PATIENTS WITH MEASURABLE METASTATIC MALIGNANT DISEASE

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PROTOCOL NUMBER(S) SFCC-78061

OBJECTIVES:

I. Determine disease specific efficacy of AD-32 in patients who have not received prior adriamycin therapy or patients who have been treated previously with adriamycin and are now resistant to adriamycin.

II. Further define acute systemic, subacute and chronic drug toxicity.

PROTOCOL ENTRY CRITERIA: Patients with measurable histologically confirmed metastatic malignant disease who are not candidates for therapy of proven clinical benefit. Disease must be refractory to other therapies, including adriamycin therapy. Patients must have recovered from all prior therapies and must have an expected survival of more than 2 months, and an ECOG performance status of 0 to 1; they should preferably have normal cardiac, renal, hepatic and hematologic function.

PROTOCOL OUTLINE:

Single-agent Chemotherapy. N-trifluoroacetyl adriamycin-14-valerate, AD-32, NSC-246131.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Liver and renal function tests.

END POINTS: Response/remission rate, toxicity/morbidity of treatment, comparability and cross resistance with Adriamycin.

CURRENT STATUS: 21 patients will be entered in 1 year.

DOSAGE SCHEDULE:

AD-32 - 600 mg/sqm iv 24-hour infusion q 21 days. Adjust dosage to cause transient leukocyte nadir of below 2000 with recovery to 4000 by day 21. To prevent vehicle toxicity administer with (AD-32) Hydrocortisone - 100 mg iv rapid infusion q 6 hours for 5 doses.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: AD-32 - 200 mg vials.

DATE SUMMARIZED: 06/79

15.0056 INDUCTION (5-FU VS 5-FU/MITO VS 5-FU PLUS RADIOTHERAPY) PLUS MAINTENANCE (5-FU VS BCG) FOR LIVER METASTASES

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PROTOCOL NUMBER(S) CA-LIVER-1

OBJECTIVES:

I. Compare randomly hepatic artery infusion chemotherapy with 5-fluorouracil vs. ia 5-fluorouracil plus mitomycin-C vs. 5-fluorouracil plus liver irradiation for effects on subjective and objective improvement, survival, and toxicity among patients with hepatic metastases from gastrointestinal and other tumors.

II. Compare randomly weekly 5-fluorouracil with an immunotherapy utilizing Glaxo-BCG for maintenance in responding patients.

III. Study nutritional support in these patients.

PROTOCOL ENTRY CRITERIA: Patients with histologically diagnosed malignant neoplasms with proven hepatic metastases. If there is extrahepatic tumor, its survival significance must be considered trivial compared with the liver disease. There may be no hepatic encephalopathy. Patients shall not have had prior liver irradiation; they must be off all chemotherapy for at least 2 weeks (6 weeks for mitomycin-C and nitrosoureas). Kidney and bone marrow function must be adequate, and there may be no evidence of hepatorenal syndrome. The life expectancy must be at least 1 month without treatment, and there may be no prior history of hepatic artery infusion.

PROTOCOL OUTLINE: Randomized study. Randomize patients to Arms I, II, and III for initial hepatic artery infusion therapy. Upon completion of initial therapy, randomize responding patients to Arms IV and V for Maintenance.

Induction

Arm I: Single-agent Hepatic Artery Infusion Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893.

Arm II: 2-Drug Combination Hepatic Artery Infusion Chemotherapy. 5-FU; Mitomycin-C, MITO, NSC-26980.

Arm III: Single-agent Hepatic Artery Infusion Chemotherapy plus Radiotherapy. 5-FU; plus hepatic irradiation.

Maintenance.

Arm IV: Single-agent Chemotherapy. 5-FU.

Arm V: Immunotherapy plus Vitamin Therapy. BCG-Glaxo, BCG, no NSC number; plus Vitamin A, NSC-122759.

STRATIFICATION BY: Site of primary (colorectal vs. other GI vs. nonGI), Karnofsky status (3-7 vs. 8-10), prior chemotherapy (yes vs. no), interval since original diagnosis (less than 8 months vs. 8 months or more), extent of metastases (small vs. large vs. extrahepatic), age (less than 60 years vs. 60-70 years vs. more than 70 years), sex, tumor differentiation (well differentiated vs. moderately well differentiated vs. poorly differentiated vs. unspecified differentiation).

SPECIAL STUDY PARAMETERS: CAT of liver and abdomen, chest x-ray, CEA, chemistry profile, serum ammonia, hematologic parameters, nutritional status, performance status.

END POINTS: Survival, response/remission rate, duration of response, toxicity/morbidity of treatment.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: 5-FU - 750 mg/sgm/day for 4 days, then 500 mg/sqm/day for 17 days by continuous infusion into the hepatic artery.

Arm II: 5-FU - 750 mg/sqm/day for 4 days then 500 mg/sqm/day for 7 days by continuous 24-hour infusion into the hepatic artery; MITO - 6 mg/sqm ia over 60 minutes on day 4 or 5 and repeat on day 9 or 10 for those patients under the age of 80 years whose pretreatment platelets were more than 200,000 and who had not received prior radiotherapy or chemotherapy.

ARM III: 5-FU - 750 mg/sqm/day for 4 days then 500 mg/sqm/day for 17 days by continuous 24-hour infusion into the hepatic artery; plus whole liver Radiotherapy - 1200 rads in 6 fractions of 200 rads over 2 weeks, escalating in groups of 3 patients as tolerated: 200 rads/day 5 days/week to a total of 1000 rads then 200 rads/day 3 days a week to a total of 1600 rads; 200 rads/day 5 days/week for a total of 2000 rads in 2 weeks.

Arm IV: 5-FU - 600 mg/sqm/week.

Arm V: BCG - id vaccination by tine technique q 2 weeks for 8 doses, then q 4 weeks for 8 doses, then q 12 weeks; Vitamin A - 30,000 U/day po.

Dosage modifications for toxicity are given.

DOSAGE FORMS: 5-FU - 500 mg vials; MITO - 5 and 20 mg vials; BÇG - 0.8-2.5 x 10 to the seventh CFU vials.

DATE SUMMARIZED: 01/81

15.0057 IMMUNOTHERAPY WITH BCG FOR ACUTE LEUKEMIA, SKIN TUMORS, SARCOMA, AND LYMPHOMA

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PROTOCOL NUMBER(S) CA-SCC-175

OBJECTIVES:

I. Outline a reliable and standard procedure for the evaluation of host immunity in patients to receive immunotherapy.

II. Describe the immunotherapy technic to be used for most of the Southern California Cancer Center tumor protocols.

PROTOCOL ENTRY CRITERIA: Patients with Stage 0-III tumors including melanoma, certain sarcomas, high-risk lymphomas in remission, adult acute leukemia in remission, lung cancer, recurrent head and neck carcinoma, and certain primary skin carcinomas. Patients may not have uncontrolled disseminated disease, active infections, or autoimmune disorders, congenital immune deficiency, or eczematous dermatosis. Liver, kidney, and bone marrow function must be adequate.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Immunotherapy. BCG-Tice, BCG, NSC-B116327.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Chest x-ray, hematologic parameters, liver function tests, CEA, quantitative immunoglobulins, skin tests.

END POINTS: Immune status, survival.

CURRENT STATUS: 28 patients have been entered as of October 1980.

DOSAGE SCHEDULE:

BCG - 10 to the eighth live organisms id by multiple puncture technic weekly for 12 weeks, then biweekly for 12 weeks, then monthly for 1 year, then bimonthly for 12 months, then trimonthly for 1 year.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

15.0058 PHASE I-II STUDY OF RADIOLABELED ANTI-CEA AND ANTI-FERRITIN IN PRIMARY LIVER CANCER, COLON CANCER, AND NON-SMALL CELL LUNG CANCER

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PROTOCOL NUMBER(S) MD-JHOC-1

OBJECTIVES:

I. Determine the maximal tolerated dose of radiolabeled antibody and the toxicities associated with treatment with I-131-labeled anti-CEA and anti-ferritin in patients with primary liver cancer, nonresectable colonic cancer, and non-small cell cancer of the lung.

II. Determine the dose distribution of radiolabeled antibody for the entire body and for the tumor.

III. Evaluate the tumor response to treatment in patients with measurable or evaluable disease.

IV. In patients with lung cancer and hepatoma, examine the dose distribution with anti-CEA and then anti-ferritin.

PROTOCOL ENTRY CRITERIA: Patients with histologically confirmed primary hepatic malignancy, non-small cell carcinoma of the lung, or colonic carcinoma with no reasonable therapeutic alternative. Patients must have measurable or evaluable disease and a Karnofsky performance status of at least 60. Patients must have adequate liver, kidney, bone marrow, cardiac, and pulmonary function. Age must be less than 75 years, and there may have been no chemotherapy, surgery, or large field radiotherapy within 28 days prior to entry. There may be no active infection and no history of asthma or eczema.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with hepatic biliary carcinoma and colonic carcinoma to Regimen A and patients with non-small cell carcinoma of the lung and hepatoma to either Regimen A or Regimen B.

Regimen A: Radiotherapy. I-131-labeled anti-CEA.

Regimen B: Radiotherapy. I-131-labeled anti-ferritin.

STRATIFICATION BY: Site of primary tumor (colon vs. lung or liver).

SPECIAL STUDY PARAMETERS: Performance status, tumor measurements, hematologic parameters, electrolytes, liver and kidney function tests, EKG, chest x-ray, pulmonary function studies, CEA, ferritin, alpha fetoprotein, T3-T4, CAT scan, radioactivity count.

END POINTS: Response/remission rate, objective tumor measurements, toxicity/morbidity of treatment, survival.

CURRENT STATUS: 10 patients have been entered as of September 1980.

DOSAGE SCHEDULE:

Regimen A: Anti-CEA - initial dose of 100 mCi iv, escalating by 50-mCi increments in groups of 3 patients of each type of tumor to the maximum tolerance dose (not to exceed 200 mCi). Allow at least 4 weeks of observation before escalating in a new group of patients.

Regimen B: Anti-ferritin - initial dosage and escalation procedures as for Anti-CEA in Regimen A.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

15.0059 ADJUVANT IMMUNOTHERAPY WITH BCG FOR CANCER OF THE KIDNEY, PROSTATE, TESTICLE, OVARY, AND UTERUS

Kerry, R. L., (313-973-2800) St. Joseph's Mercy Hospital, P.O. Box 995, Ann Arbor, Michigan, 48106, United States of America

PROTOCOL NUMBER(S) MI-GI-1

OBJECTIVES:

I. Determine whether immunotherapy with Tice BCG will improve the remission time and cure rate of patients with cancer of the genitourinary tract.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven cancer, with or without prior surgery (adjuvant) or known residual disease.

PROTOCOL OUTLINE: Randomized study.

Arm I: Immunotherapy. Tice BCG, BCG, NSC-B116327.

Arm II: No further treatment.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be admitted.

DOSAGE SCHEDULE:

Arm I: BCG - 1 ampule per two sites (groins) by multiple-puncture tine technique initially; then weekly vaccinations in both axillae and both groin areas for 12 weeks, then monthly for remainder of 2 years.

Arm II: No treatment.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - 2-8 x 10 to the eighth colony-forming-units/ampule.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

15.0060 SURGERY WITH AND WITHOUT IMMUNOTHERAPY WITH BCG FOR HIGH-RISK OR MULTIPLE CANCER

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PROTOCOL NUMBER(S) MI-HR-1

OBJECTIVES:

I. Determine whether vaccination with BCG-Tice will improve the incidence or cure rate of patients with a 'high risk' of developing cancer.

II. Determine whether the time of initiation of the BCG program influences the response and whether less frequent vaccinations than those customarily used will be as effective as the other protocols being used.

PROTOCOL ENTRY CRITERIA: Patients with primary cancer or high risk of developing cancer (a 30% or greater chance). Lesions present at time of entry will be excised.

PROTOCOL OUTLINE: Randomized study.

Arm I: Surgery plus Immunotherapy. BCG-Tice, BCG, NSC-B116327.

Arm II: Surgery.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Immunocompetence status.

END POINTS: Recurrence/response rate, survival rate, length of survival, toxicity/morbidity of treatment.

CURRENT STATUS: Up to 50 patients will be entered.

DOSAGE SCHEDULE:

Arm I: Surgery, followed by BCG - 1 ampule divided among 4 sites, both axillae and groin areas, by multipuncture tine technique, weekly for 4 doses. After 4 weeks, monthly treatment for 5 years.

Arm II: Surgery only.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: BCG - ampules containing 2-8 x 10 to the eighth colony-forming units.

Summary as provided by investigator.

DATE SUMMARIZED: 04/80

15.0061 COMBINATION CHEMOTHERAPY (CTX/VCR/ACT-D OR VBL/BLEO/CACP) AND/OR RADIOTHERAPY FOR MALIGNANT GERM CELL TUMORS IN CHILDREN

Brodeur, G. M., (901-522-0500) St. Jude Childrens Research Hospital, 332 N. Lauderdale St., P.O. Box 318, Memphis, Tennessee, 38101, United States of America
PROTOCOL NUMBER(S) SJCRH-GCT-79

OBJECTIVES:

I. Provide a plan for uniform staging, treatment, and followup of children with malignant germ cell tumors.

II. Compare the 2-year disease-free survival rate in Stage III and IV disease with historical results.

III. Determine the pharmacokinetics and renal toxicity of cis-platinum in children given a 2-hour infusion compared to those given a 6-hour infusion in a Phase II cis-platinum study.

IV. Evaluate the relative efficacy of different modalities of diagnostic imaging in the staging and followup of patients with malignant germ cell tumors.

PROTOCOL ENTRY CRITERIA: Previously untreated patients under the age of 20 years with a biopsy-proven germ cell malignancy.

PROTOCOL OUTLINE: Nonrandomized study. Enter patients with Stage I-III pure germinoma ovarian tumors to Radiotherapy Regimen C and those with Stage IV disease to Regimen A. Enter all non-germinoma type ovarian tumor patients to Regimen A, with optional Radiotherapy for Stages III and IV. If no response after 2 courses of Chemotherapy or if less than partial response after 4 courses, cross over to Regimen B. If partial but less than complete response after 4 courses, add Radiotherapy. Of patients with testicular or extragonadal germ cell tumors to be treated with Chemotherapy, enter patients under the age of 10 years to Regimen A and those 10 years of age and older to Regimen B. Patients with Stage I-III pure germinoma testicular tumors will be treated with Radiotherapy and Stage IV patients with Chemotherapy. Non-germinoma testicular tumor patients will receive no further treatment for Stage I and Chemotherapy for Stage II-IV. If no response after 2 courses, or if less than partial response after 4 courses, cross over to alternate Chemotherapy. If partial but not complete response after 4 courses, add Radiotherapy. Patients with Stage I-III extragonadal pure germinomas will be treated with Radiotherapy; patients with Stage IV disease and all patients with non-germinoma extragonadal tumors will be treated with Chemotherapy. If no response after 2 courses, or less than partial response after 4 courses, cross over to alternate Chemotherapy. If partial but not complete response after 4 courses, add Radiotherapy.

Regimen A: 3-Drug Combination Chemotherapy. Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; Actinomycin-D, ACT-D, NSC-3053.

Regimen B: 3-Drug Combination Chemotherapy. Vinblastine, VBL, NSC-49842; Bleomycin, BLEO, NSC-125066; cis-Platinum, CACP, NSC-119875.

Regimen C: Radiotherapy. No details given.

STRATIFICATION BY: Age (less than 10 years vs. 10 years and older), site of primary tumor (ovarian vs. testicular vs. extragonadal), stage of disease (I vs. II vs. III vs. IV).

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, electrolytes, coagulation screen, immunoglobulins, alpha-fetoprotein, beta human chorionic gonadotropin, chest x-ray, IVP, bone scan, liver scan, gallium scan, ultrasound, CT, bone marrow aspiration.

END POINTS: Response/remission rate, duration of response, disease-free interval, recurrence rate, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: 25-30 patients will be entered in 3-4 years.

DOSAGE SCHEDULE:

Regimen A: CTX - 100 mg/sqm/day po on days 1 through 7; VCR - 1.5 mg/sqm (maximum 2.0 mg) iv on day 8; ACT-D - 1.5 mg/sqm (maximum 2.0 mg) iv oon day 8. Repeat at 4-week intervals for a total of 12 courses.

Regimen B: VBL - 6 mg/sqm iv on day 1 q 3 weeks for 6 courses, then 6 mg/sqm iv on day 1 and 3-6 mg/sqm iv on day 2 q 3 weeks for 10 courses; BLEO - 30 U/sqm iv q 3 weeks for 6 courses; CACP - 500 mg/sqm iv over 2 hours, with adequate prehydration and mannitol diuresis, q 3 weeks for 6 courses.

Regimen C: Radiotherapy. No details given.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 01/81

15.0062 SEQUENTIAL SYNCHRONIZATION CHEMOTHERAPY WITH BLEOMYCIN AND VM-26 FOR REFRACTORY B-CELL LYMPHOMA AND LEUKEMIA IN CHILDREN

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PROTOCOL NUMBER(S) SJCRH-NHL-B

OBJECTIVES:

I. Produce complete remission of refractory or recurrent B-cell lymphoma and leukemia in children using bleomycin and VM-26 sequentially.

II. Synchronize lymphoma cells in vivo by a continuous infusion of bleomycin and determine the validity of a combined cell kinetic and pharmacokinetic model of drug action by the serial estimation of tumor cell cycle compartment distributions and plasma bleomycin levels.

III. Increase tumor cell killing by the timed application of a second cell cycle specific drug, VM-26, at a time of maximum accumulation of target cells in a sensitive phase of the cell cycle.

Measure the effectiveness of this sequential combination by clinical observation of oncolytic responses and by the measured mitotic inhibition and G2 arrest of tumor cells produced by VM-26.

PROTOCOL ENTRY CRITERIA: Children with refractory or recurrent B-cell lymphoma or leukemia who fail treatment on a first-line protocol. Patients must have adequate renal function.

PROTOCOL OUTLINE: Nonrandomized study.

2-Drug Combination Chemotherapy. Bleomycin, BLEO, NSC-125066; VM-26, NSC-122819.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters; bone marrow aspiration for differential smears, surface markers, and kinetic studies; liver and kidney function tests; electrolytes; chest x-ray; abdominal and pelvic ultrasound; additional diagnostic x-rays as clinically indicated; cytology, surface markers, and kinetic studies of tumor cells aspirated from malignant pleural or peritoneal effusions (if present).

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: At least 10-13 patients should be entered.

DOSAGE SCHEDULE:

BLEO - 2 U/sqm iv push followed immediately by 30 U/sqm/24 hours in a continuous 48-hour iv infusion; VM-26 - 250 mg/sqm iv over 30 minutes, beginning immediately at the conclusion of the BLEO infusion. Repeat courses q 96 hours until CR, progressive disease, or intolerable toxicity. Once CR is achieved, allow time for recovery from toxicity and give 1 course q 2 weeks until total cumulative dose of BLEO is 372-496 U/sqm (6-8 complete courses).

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

15.0063 PHASE II COMBINATION CHEMOTHERAPY PLUS SUPERFRACTIONATED RADIOTHERAPY FOR B-CELL NON-HODGKIN'S LYMPHOMA AND B-CELL ACUTE LEUKEMIA IN CHILDREN

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PROTOCOL NUMBER(S) SJCRH-NHL-79-III/IV

OBJECTIVES:

I. Achieve prolonged continuous complete remission and cure in children with Stage III-IV B-cell non-Hodgkin's lymphoma (NHL) using superfractionated radiotherapy plus combination chemotherapy with cyclophosphamide, cytosine arabinoside, adriamycin, vincristine, and it methotrexate/cytosine arabinoside (MAIT).

II. Assess the toxicity of this combined modality treatment.

PROTOCOL ENTRY CRITERIA: Children presenting with Stage III-IV B-cell NHL with extensive unresectable intra-abdominal lymphoma or other prominent extranodal disease, often apparently multicentric, involving, e.g., jaws, gonads, or epidural space; patients with B-cell acute lymphocytic leukemia with L3 immunoblastic morphology; and patients relapsed from treatment for B-cell NHL with a good prognosis.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Single-agent Systemic Chemotherapy plus 2-Drug Combination Intrathecal Chemotherapy plus Citrovorum Rescue. Cyclophosphamide, CTX, NSC-26271; plus MAIT: Methotrexate, MTX, NSC-740; Cytosine arabinoside, ARA-C, NSC-63878; plus Citrovorum Factor, CF, NSC-3590.

Regimen B: Radiotherapy plus 2-Drug Combination Intrathecal Chemotherapy. 4 MeV Linear Accelerator; plus MAIT.

Regimen C: Single-agent Systemic Chemotherapy plus 2-Drug Combination Intrathecal Chemotherapy. ARA-C; plus MAIT.

Regimen D: 2-Drug Combination Systemic Chemotherapy plus 2-Drug Combination Intrathecal Chemotherapy. Adriamycin, ADR, NSC-123127; Vincristine, VCR, NSC-67574; plus MAIT.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, immunoglobulins, serum protein immunoelectrophoresis, fibrinogen, coagulation screen, bone marrow aspiration, CSF examination, chest x-ray, IVP, skeletal survey, pantomograms of mandible and maxilla, whole body gallium scans, tuberculin and histoplasmin skin tests.

END POINTS: Response/remission rate, duration of response, survival, duration of survival, toxicity/morbidity of treatment.

CURRENT STATUS: 30-50 patients will be entered over 2-3 years.

DOSAGE SCHEDULE:

Regimen A: CTX - 300 mg/sqm iv push at time 0 and repeated q 12 hours for a total of 6 doses; MAIT: MTX - 10 mg/sqm, and ARA-C - 50 mg/sqm on day 0; CF - 3 mg po q 6 hours beginning 24 hours after MAIT. Assess tumor response and proceed to Regimen B after marrow recovery (14-21 days).

Regimen B: Radiotherapy. 4 MeV Linear Accelerator - 1800 rads to the CNS and simultaneously 2250 rads to the primary site in 18 fractions, 2 fractions per day, 6 days per week. Assess tumor response following recovery from acute effects of Radiotherapy. If patient is in CR, proceed to Regimen C; if resistant or recurrent disease is found systemically, repeat Regimen A after adequate recovery from Radiotherapy.

Regimen C: ARA-C - 150 mg/sqm/day in continuous 72-hour iv infusion; MAIT plus CF - as in Regimen A at the beginning of ARA-C infusion. After 14-21 days of recovery, proceed to Regimen D.

Regimen D: VCR - 1.5 mg/sqm/week iv for 3 doses; ADR - 50 mg/sqm iv with first and third dose of VCR; MAIT and CF as in Regimen A. Repeat Regimens C and D with appropriate intervals for recovery from toxicities.

CNS disease manifest at diagnosis should be treated with MAIT once or twice weekly until the beginning of Regimen B. Suspected testicular disease should be proven by biopsy and treated with 1500-2000 rads.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

15.0064 PHASE II CHEMOTHERAPY WITH PIPERAZINEDIONE IN ACUTE CHILDHOOD LEUKEMIA AND SOLID TUMORS

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PROTOCOL NUMBER(S) SJCRH-PIPER-2

OBJECTIVES:

I. Determine antineoplastic and toxic effects of piperazinedione in children with acute leukemia and solid tumors refractory to conventional chemotherapeutic agents.

PROTOCOL ENTRY CRITERIA: Children with acute leukemia or solid tumors with measurable parameters of disease activity, resistant to conventional agents and requiring no radiotherapeutic measures that might interfere with evaluation of the chemotherapeutic program. Liver and renal functions as well as nutritional status must be satisfactory.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. Piperazinedione, PZD, NSC-135758.

STRATIFICATION BY: Not given.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, objective tumor response, survival rate, length of survival.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

For acute leukemia: PZD - 5 mg/sqm/day iv for 5 days. For solid-tumors: PZD - 3 mg/sqm/day for 5 days. Repeat course at intervals of 14 to 21 days for a minimum of 8 weeks.

DOSAGE FORMS: PZD - 10 ml vials.

DATE SUMMARIZED: 12/77

15.0065 TOTAL THERAPY OF HIGH-RISK CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA AND NON-HODGKIN'S LYMPHOMA WITH VM-26, MTX, L-ASP, VCR, PRED, ARA-C AND 6-MP

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PROTOCOL NUMBER(S) SJCRH-TOT-X-HR

OBJECTIVES:

I. Determine whether administration of VM-26 plus cytosine arabinoside prior to standard Induction chemotherapy with prednisone/vincristine/L-asparaginase will increase the frequency and duration of remission in children with 'high-risk' acute lymphocytic leukemia and non-Hodgkin's lymphoma (NHL).

II. Determine whether intrathecal therapy alone with methotrexate is effective in preventing CNS leukemia during the first year of therapy.

III. Determine the incidence of histologic testicular leukemia following one year of complete clinical remission.

PROTOCOL ENTRY CRITERIA: Previously untreated children with acute lymphocytic leukemia who have one or more of the following findings at diagnosis: mediastinal mass, WBC over 100,000, CNS leukemia, leukemia cells that form heat stable rosettes with sheep erythrocytes. Patients who have had up to 10 days of any prior therapy and Induction failures from standard-risk protocols will also be eligible. Previously untreated patients with lymphoblastic lymphomas who have a mediastinal mass or generalized nodal disease (Stages III-IV) with or without pleural effusion, CNS disease at diagnosis, or bone marrow involvement will be eligible. Patients who have had up to 10 days of prior therapy will be eligible.

PROTOCOL OUTLINE: Nonrandomized study.

Regimen A: Induction. 4-Drug Combination Chemotherapy plus Hormone Therapy. VM-26, NSC-122819; Cytosine arabinoside, ARA-C, NSC-63878; Vincristine, VCR, NSC-67574; L-Asparaginase, L-ASP, source not specified; plus Prednisone, PRED, NSC-10023.

Regimen B: CNS Prophylaxis. Single-agent Intrathecal Chemotherapy plus Radiotherapy. Methotrexate, MTX, NSC-740; Co-60 or linear accelerator.

Regimen C. Maintenance. 2-Drug Alternating Combination Chemotherapies. 6-Mercaptopurine, 6-MP, NSC-755; MTX; alternating with VM-26; ARA-C.

STRATIFICATION BY: CNS disease at diagnosis (yes vs. no).

SPECIAL STUDY PARAMETERS: Hematologic parameters, liver and kidney function tests, electrolytes, hepatitis B surface antigen, coagulation screening, bone marrow aspiration (for cytology, cytochemistry, surface markers, steroid receptors, karyotype analysis), CSF examination, thoracentesis for cytology and surface marker studies on cells in pleural effusions, chest x-ray, EKG, EEG, microbiological cultures, histoplasmin and intermediate PPD skin tests, IVP, skeletal survey, brain scan.

END POINTS: Response/remission rate, duration of response, survival, toxicity/morbidity of treatment.

CURRENT STATUS: About 50 patients with newly diagnosed acute lymphocytic leukemia, 15 with NHL, and 25 failures from a standard-risk acute lymphocytic leukemia protocol are expected to be entered within 3 years.

DOSAGE SCHEDULE:

Regimen A: VM-26 - 165 mg/sqm/week iv on weeks 1, 2, 7, and 8; ARA-C - 300 mg/sqm/week iv on weeks 1, 2, 7, and 8; PRED - 40 mg/sqm/day po on weeks 3 through 6; VCR - 1.5 mg/sqm/week (maximum 2.0 mg) iv on weeks 3 through 6; L-ASP - 10,000 U/sqm iv twice weekly on weeks 3 through 6.

Regimen B: MTX - 12 mg/sqm (maximum 12 mg) it at the time of diagnostic marrow and q 2 weeks during Induction for a total of 5 doses by the expected M1 date; thereafter, q 10 weeks during Maintenance until 52 weeks of complete clinical remission; 2400 rads cranial irradiation (2000 rads for infants under age 2 years) in 14-15 fractions through opposing lateral ports including the retro-orbital space and the first two cervical vertebrae, plus 5 doses of it MTX over 2.5 weeks commencing at the conclusion of Maintenance therapy. Patients with CNS disease at diagnosis or during Induction receive weekly it MTX until the CSF is clear for 2 consecutive weeks, then monthly until 52 weeks after the M1 date, at which time 3000 rads of craniospinal irradiation will be given.

Regimen C: 6-MP - 50 mg/sqm/day po for 8 weeks; MTX - 40 mg/sqm/week po for 8 weeks; VM-26 - 165 mg/sqm iv twice weekly for 2 weeks following 6-MP/VM-26; ARA-C - 300 mg/sqm iv twice weekly for 2 weeks following 6-MP/VM-26. Repeat this 10-week cycle 5 times, giving it MTX (Regimen B) prior to each 2-week course of VM-26/ARA-C. Reassess after 52 weeks, and administer delayed CNS prophylaxis (Regimen B). Then continue on 6-MP plus MTX only for the next 1.5 years (total of 2.5 years of therapy).

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/80

15.0066 EVALUATION OF THE PYROGENIC AND POSSIBLY IMMUNOGENIC PROPERTIES OF C. PARVUM IN PATIENTS WITH ADVANCED MALIGNANCIES

Stehlin, J. S., (713-652-3161) The Stehlin Foundation for Cancer Research, 777 St. Joseph Prof. Bldg., Houston, Texas, 77002, United States of America

PROTOCOL NUMBER(S) TX-SFCR-114686K

OBJECTIVES:

I. Study the possible therapeutic efficacy of C. parvum administered singly or with various chemotherapeutic agents in patients with advanced malignancies.

PROTOCOL ENTRY CRITERIA: Patients with advanced melanoma, carcinoma, and sarcoma.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy with or without Single-agent Chemotherapy. C. parvum unspecified, no NSC number; alone or with DTIC, NSC-45388; 5-Fluorouracil, 5-FU, NSC-19893; Methotrexate, MTX, NSC-740; Vincristine, VCR, NSC-67574; Cyclophosphamide, CTX, NSC-26271; Actinomycin-D, ACT-D, NSC-3053; Adriamycin, ADR, NSC-123127; or Bleomycin, BLEO, NSC-125066.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: None given.

END POINTS: Duration of survival.

CURRENT STATUS: 190 patients were entered as of September 1980.

DOSAGE SCHEDULE:

C. parvum - 1-2 mg/sqm/day iv for 5-10 days, alone or in combination with chemotherapeutic agents, depending on individual patients.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

Summary as provided by investigator.

DATE SUMMARIZED: 01/81

15.0067 PHASE II CHEMOTHERAPY WITH AMSA FOR ACUTE LEUKEMIA OR RELAPSED LYMPHOMA

Pavlovsky, S., (821-8803) Pan American Health Org., Collaborative Cancer Treatment & Research Program, c/o Hospital Central Militar, Buenos Aires, Argentina

PROTOCOL NUMBER(S) ARG-DSI-7902

OBJECTIVES:

I. Examine the use of AMSA in acute leukemias and Hodgkin's and non-Hodgkin's lymphoma relapsed from prior therapy.

PROTOCOL ENTRY CRITERIA: Patients with measurable acute leukemia or lymphoma who have relapsed following standard therapy.

PROTOCOL OUTLINE: Nonrandomized study. Single-agent Chemotherapy. AMSA, NSC-249992.

STRATIFICATION: Participating institutions, disease type.

SPECIAL STUDY PARAMETERS: Liver function, bone marrow aspirate.

END POINTS: Response/remission rate, objective tumor response, toxicity/morbidity of treatment.

CURRENT STATUS: 50 patients will be entered in 1 year.

DOSAGE SCHEDULE:

For acute leukemia: AMSA - 75 to 90 mg/sqm iv over 30 to 60 min on days 1 through 7 q 2 weeks.

For lymphoma: 40 mg/sqm iv on days 1 through 3 q 4 weeks.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: AMSA - 75 mg ampules.

DATE SUMMARIZED: 12/79

15.0068 PHASE I AND II IMMUNOTHERAPY WITH BCG-MER FOR DIVERSE NEOPLASMS

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PROTOCOL NUMBER(S) ARG-RNH-4002

OBJECTIVES:

I. Determine the maximum tolerated dosage of intradermal BCG-MER in patients with diverse neoplasms.

II. Determine the proper dosage of BCG-MER, its local effects, systemic toxicity, and effects on various immunological parameters.

III. Determine the changes in tolerance of normal tissues and the immunopotentiating and immunotherapeutic activity of BCG-MER.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven diagnosis of a neoplasm, with a life expectancy of at least 3 months upon entry and with Karnofsky performance status of at least 50%. Patients may not have had prior immunotherapy or chemotherapy, and must be without signs of systemic infection. Patients must have acceptable blood counts and liver and kidney functions. Long-term followup must be feasible.

PROTOCOL OUTLINE: Nonrandomized study.

Immunotherapy. BCG-MER, MER, NSC-143769.

STRATIFICATION BY: None given.

SPECIAL STUDY PARAMETERS: Lymphoblastogenesis with PHA, lymphocyte rosette inhibition test, serum immunoglobulins by radical immunosuppression, cutaneous tests of skin hypersensitivity, determination of serum complement fraction by C3.

END POINTS: Toxicity/morbidity of treatment.

CURRENT STATUS: 60 patients will be admitted.

DOSAGE SCHEDULE:

MER - 500, 1000, or 2000 mcg id in 5 divided doses (100, 200, or 400 mcg each, respectively) at 5 different sites on one of two different schedules: (1) weekly for 8 weeks; or (2) q 15 days for 8 cycles. Thereafter, treatment is given monthly, in decreasing doses, to determine the dose that produces a 1-cm lesion with minimal central necrosis. At that dose, treatment is continued indefinitely (minimum 12 months).

Dosage modifications for toxicity are given.

DOSAGE FORMS: MER-BCG - 500 mcg ampules.

DATE SUMMARIZED: 08/80

15.0069 PILOT CHEMOTHERAPY WITH FAP (5-FU/ADR/CACP) FOR ADVANCED ADENOCARCINOMA OF THE LUNG, STOMACH AND PANCREAS

Estevez, R., Pan American Health Org., Collaborative Cancer Research Project, c/o Hospital Central Militar, Buenos Aires, Argentina

PROTOCOL NUMBER(S) ARG-7901

OBJECTIVES:

I. Undertake a one arm pilot study of FAP - 5-fluorouracil (5-FU), adriamycin (ADR) and cis-platinum (CACP) for advanced measurable adenocarcinoma of the lung, stomach and pancreas.

II. Compare results with historical data.

PROTOCOL ENTRY CRITERIA: Previously untreated patients 14 to 75 years of age with biopsy-proven, measurable advanced adenocarcinoma of the lung, stomach, or pancreas. Patients must have adequate renal function (creatinine clearance above 60 ml/min).

PROTOCOL OUTLINE: Nonrandomized study.

3-Drug Combination Chemotherapy. 5-Fluorouracil, 5-FU, NSC-19893; Adriamycin, ADR, NSC-123127; cis-Platinum, CACP, NSC-118975.

STRATIFICATION: Not given.

SPECIAL STUDY PARAMETERS: Liver scan; CAT scan - if appropriate and available.

END POINTS: Objective tumor responses, response/remission rate; duration of response; toxicity/morbidity of treatment; survival time.

CURRENT STATUS: 60 patients will be entered.

DOSAGE SCHEDULE:

5-FU - 600 mg/sqm iv on days 1 and 8; ADR - 30 mg/sqm (500 mg/sqm maximum cumulative dose) iv on day 1; CACP - 75 mg/sqm iv four hour infusion on day 1 with adequate hydration. Repeat course q 28 days until disease progression, development of unacceptable toxicity or until complete remission is achieved.

Dosage modifications for toxicity and for impaired liver function are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/79

15.0070 CIS-PLATINUM/BLEOMYCIN WITH OR WITHOUT BCG IMMUNOTHERAPY FOR EPIDERMOID CARCINOMA OF THE HEAD AND NECK, CERVIX OR PENIS

Gentil, F., (Sao Paulo 278-8811) Fundacao A.C. Camargo, Rua Prof. Antonio Prudenti 211, Postal Box 5271, Sao Paulo 01509, Brazil

PROTOCOL NUMBER(S) BRA-EPI-7703

OBJECTIVES:

I. Determine the quality and duration of response of epidermoid carcinomas of several origins, assess the influence of the immunological status on the prognosis, and determine the value of oral BCG administration in improving the quality and duration of response.

II. Evaluate the possibility of increasing the presently dismal cure rates in locally advanced epidermoid carcinomas, by means of a multidisciplinary approach: Chemotherapy with cis-platinum (CACP)/bleomycin (BLEO) plus Immunotherapy, surgery, or radiation therapy.

PROTOCOL ENTRY CRITERIA: Patients under 60 years old with measurable epidermoid carcinoma of the head and neck, cervix or penis. Patients must have no prior Chemotherapy or Immunotherapy and a performance status of at least 60. Patients must have adequate renal and auditory function.

PROTOCOL OUTLINE: Randomized study.

Arm I: 2-Drug Combination Chemotherapy. cis-Platinum, CACP, NSC-119875; Bleomycin, BLEO, NSC-125066.

Arm II: 2-Drug Combination Chemotherapy plus Immunotherapy. CACP, BLEO; BCG-Moreau, in Brazil (or BCG, NSC-B116341).

STRATIFICATION BY: Participating institutions, disease sites.

SPECIAL STUDY PARAMETERS: Spirometry, audiometry, skin tests for recall antigens.

END POINTS: Objective tumor response, toxicity/morbidity of treatment, response/remission rate, response duration, quality of response.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: CACP - 80 mg/sqm iv with hydration and diuresis on day 1; BLEO - 15 mg/sqm iv on days 1 through 5. Repeat course q 3 or 4 weeks.

Arm II: CACP, BLEO as in Arm I; BCG - 600 mg po on days 12 through 17. Repeat course q 3 or 4 weeks.

Continue therapy for 1 year after complete response or until relapse or the development of unacceptable toxicity.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 12/78

PATIENT ACCRUAL: 00071078

15.0071 PHASE II LOW-DOSE COMBINATION CHEMOTHERAPY WITH DDMP/CF FOR EPIDERMOID CARCINOMA, RENAL CELL CARCINOMA, MELANOMA, AND SOFT TISSUE SARCOMA

Alberto, P., (Geneva (022) 29-18-18) European Org. for Research on Treatment of Cancer, Early Clinical Trials Cooperative Group, Swiss Group for Clinical Cancer Research, 62 Rue de Carouge, 1205 Geneva, Switzerland
PROTOCOL NUMBER(S) EORTC-16771

OBJECTIVES:

I. Explore the antitumor activity of DDMP given concurrently with a low-dose citrovorum factor (CF) rescue in patients with epidermoid tumors, melanoma, renal cell carcinoma, or soft tissue sarcomas.

II. Assess the tolerance of the treatment schedule.

III. Define the nature, duration, reversibility and treatment of drug-related toxicity.

PROTOCOL ENTRY CRITERIA: Patients over 15 years of age with histologically diagnosed measurable or evaluable progressive disease of epidermoid carcinoma of the head and neck, lung, or any other known origin, melanoma, renal cell carcinoma, and soft tissue sarcoma. Patients must not have had treatment with trimethoprim within one month, or other therapy within 3 weeks of present treatment except for limited palliative radiation therapy. Patients must have a Karnofsky index of 40 or more with adequate renal, hepatic, and hematological function.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy plus Rescue, DDMP, NSC-19494; Citrovorum factor, CF, NSC-3590.

STRATIFICATION BY: Tumor type.

SPECIAL STUDY PARAMETERS: Not given.

END POINTS: Response/remission rate, duration of response, toxicity/morbidity of treatment, recurrence rate.

CURRENT STATUS: 14 to 25 patients will be entered in each stratification.

DOSAGE SCHEDULE:

CF - 3 mg im or iv given q 7 days immediately before DDMP; 25 mg/sqm po or 50 mg/sqm up to 1.5 sqm body surface; 75 mg/sqm between 1.6 - 2.0 sqm body surface; 100 mg/sqm for more than 2 sqm body surface. Provide adequate hydration.

In case of toxicity discontinue DDMP during rescue time and increase CF rescue to 15 mg iv or im q 6 hours for 3 days. After recovery resume CF - 9 mg/week immediately befor DDMP at original dose. In case of repeated toxicity increase CF to 15 mg/week. Treat patients with primary progression for 6 weeks. Treat patients with regression of stabilization of disease until relapse.

Dosage modifications for toxicity are given.

DOSAGE FORMS: DDMP - 25 mg tablets.

DATE SUMMARIZED: 05/79

15.0072 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED LYMPHOMAS AND SOLID TUMORS

De Jager, R., European Org. for Research on Treatment of Cancer, Early Clinical Trials Coop. Grp., Institut Jules Bordet, 1 Rue Heger-Bordet, 1000 Bruxelles, Belgium
PROTOCOL NUMBER(S) EORTC-16791

OBJECTIVES:

I. Evaluate the antitumor activity of m-AMSA in advanced lymphomas and solid tumors.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven lymphomas: Hodgkin's disease or malignant lymphoma of high-grade malignancy (lymphocytic poorly differentiated, histiocytic diffuse, and undifferentiated); or histologically proven solid tumors of the following types: head and neck epidermoid carcinoma, carcinoma of the lung, breast carcinoma, gastro-intestinal tract adenocarcinoma, testicular cancer, cervix uteri epidermoid carcinoma, carcinomas of the kidney, or melanoma. Patients must have advanced, measurable or evaluable disease and not be candidates for well established, potentially curative or palliative treatment. Patients must be under 75 years of age; they must have adequate hematologic, renal, and hepatic function and a Karnofsky performance status of at least 40. Patients must not have a second tumor (except cured skin cancer) nor have received chemotherapy for at least 21 days prior to entry.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. m-AMSA, AMSA, NSC-249992.

STRATIFICATION BY: Tumor type, participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurements; chest x-ray; bone scan; x-rays of symptomatic areas; EKG; hematologic, renal, and hepatic function tests; radioisotopic scans.

END POINTS: Response/remission rate, duration of response, disease-free interval, objective tumor response, survival rate, toxicity/morbidity of treatment.

CURRENT STATUS: 14 patients will be entered in each tumor type.

DOSAGE SCHEDULE:

m-AMSA - 120 mg/sqm (90 mg/sqm for patients with extensive prior chemotherapy) iv for 60 minutes, q 3 weeks. A minimum of 2 courses should be given. Patients with an objective response continue treatment until progression.

Dosage modifications for toxicity are given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 10/80

15.0073 PHASE II CHEMOTHERAPY WITH NORGAMEM FOR EPIDERMOID CANCER OF THE HEAD AND NECK AND LUNG

Alberto, P., (Geneve 22-469211) European Org. for Research on Treatment of Cancer, Early Clinical Trials Group, Hopital Cantonal, 24 Rue Micheli du Crest, 1205 Geneve, Switzerland
PROTOCOL NUMBER(S) EORTC-16801

OBJECTIVES:

I. Define the antitumor activity of L-4 thiazolidine carboxylic acid (Norgamem) in epidermoid carcinoma.

PROTOCOL ENTRY CRITERIA: Patients with histologically proven epidermoid carcinoma of the head and neck and lung, measurable disease (pleural effusion, osseous, and CNS metastases are not acceptable as a measurable lesion). Patients must have a Karnofsky status of at least 50 and no previous chemotherapy. Patients with previous radiotherapy must have progressive disease and no therapy for 4 months prior to entry. Patients must not have active infection, severe malnutrition, another different primary tumor, senility, psychosis, or CNS disease.

PROTOCOL OUTLINE: Nonrandomized study.

Single-agent Chemotherapy. L-4 Thiazolidine carboxylic acid, Norgamem, NSC-25855.

STRATIFICATION BY: Participating institutions.

SPECIAL STUDY PARAMETERS: Tumor measurement; hematologic, renal, and hepatic function tests.

END POINTS: Response/remission rate, objective tumor response, survival length.

CURRENT STATUS: 14 patients will be entered in each tumor type; for each response, additional patients will be entered.

DOSAGE SCHEDULE:

Norgamem - 40 mg/kg im daily in 4 equal doses q 6 hours. Patients should be treated for a minimum of 6 weeks; those showing CR continue treatment for 4 months; those with progressive disease or life-endangering toxicity go off study.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Norgamem - 250 mg vials.

DATE SUMMARIZED: 10/80

15.0074 TOTAL BODY IRRADIATION VS CHEMOTHERAPY WITH CLB/PRED FOR CHRONIC LYMPHOCYTIC LEUKEMIA AND LYMPHOCYTIC LYMPHOMA

Jacobs, P., (Cape Town 47-5390) University of Cape Town
Medical School, Dept. of Haematology, Anzio Road,
Observatory 7925, Cape Town, South Africa

PROTOCOL NUMBER(S) SAFR-CT-LEU/LYM-B

OBJECTIVES:

I. Determine the efficacy of total body irradiation or chemotherapy with chlorambucil/prednisone in patients with CLL or lymphocytic lymphoma.

PROTOCOL ENTRY CRITERIA: Patients with chronic lymphocytic leukemia (absolute lymphocytosis must be greater than 15 x 10 to the ninth/liter), or Stage III and IV lymphocytic lymphoma: follicular lymphoma (all cell types) and small cell diffuse (well differentiated) lymphoma. Patients with lymphocytic lymphoma must have relapsed after less than 1 year of treatment on protocol SAFR-CT-LEU/LYM-A.

PROTOCOL OUTLINE: Patients with chronic lymphocytic leukemia, follicular lymphoma (all cell types) and small cell diffuse (well differentiated) disease are stratified according to histological classification and randomized to Arms I and II. Patients with follicular lymphoma and those with small cell diffuse (well differentiated) lymphocytic lymphoma who fail on either Arm I or II enter Regimen A. Failures on Regimen A proceed to Regimen B. Any of these patients with pancytopenia at diagnosis or at any time during treatment are treated on Regimen C. Any patients who may benefit from splenectomy will initially undergo Surgery.

Arm I: Radiotherapy. Total body irradiation.

Arm II: Single-agent Chemotherapy plus Hormone Therapy. Chlorambucil, CLB, NSC-3088; plus Prednisone, PRED, NSC-10023.

Regimen A: 2-Drug Combination Chemotherapy plus Hormone Therapy. COP: Cyclophosphamide, CTX, NSC-26271; Vincristine, VCR, NSC-67574; plus PRED.

Regimen B: 3-Drug Combination Chemotherapy plus Hormone Therapy. CHOP: CTX; ADR; VCR; plus PRED.

Regimen C: 2-Drug Combination Chemotherapy plus Hormone Therapy. BOP: Bleomycin, BLEO, NSC-125066; VCR; plus PRED.

STRATIFICATION BY: Chronic lymphocytic leukemia vs. follicular lymphoma (all cell types) vs. small cell-diffuse (well differentiated) lymphoma.

SPECIAL STUDY PARAMETERS: Cytochemical studies of blood and bone marrow, immunologic classification, functional characteristics of lymphocytes.

END POINTS: Response/remission rate, the relationship of response to survival, quality of life, immune competence.

CURRENT STATUS: Not given.

DOSAGE SCHEDULE:

Arm I: TBI - 15 rads 2 times a week to a total of 150 rads.

Arm II: CLB - 2-12 mg/day po in 3 divided doses; PRED - 0.5 mg/kg (maximum dose 30 mg) po daily for a month.

Regimen A: COP: CTX - 500 mg/sqm or 15 mg/kg iv once a week; VCR - 1.5 mg/sqm (maximum dose 2 mg) iv once a week; PRED - 30 mg po daily for 6 weeks. Treatment is continued for 6 weeks.

Regimen B: CHOP: CTX - 750 mg/sqm iv on day 1; ADR - 40 mg/sqm on day 1; VCR - 1.4 mg/sqm iv on days 1 and 8; PRED - 45 mg/sqm po daily for 10 days.

Regimen C: BOP: BLEO - 20 mg/sqm plus VCR - 1.4 mg/sqm weekly for 6 doses; PRED - 30 mg/sqm po daily for 1 month.

Dosage modifications for toxicity are not given.

DOSAGE FORMS: Not given.

DATE SUMMARIZED: 01/81

SECTION 16

PHASE I PROTOCOLS

This section was created in response to an expressed need by investigators for information on protocols of new cancer therapy agents at the earliest stages of development. It consists of a brief, preliminary list of several Phase I protocols activated during 1980.

SINGLE AGENTS

Aclacinomycin

NSC-208734

Protocol #	**Principal Investigator**	**Address**
(NCI)W80-101	Franco, L. 313-577-1818	Wayne State University, Department of Oncology, 3990 John R Street, Detroit, MI 48201
(NCI)W80-167	Neidhart, J.A. 614-422-5317	Ohio State University Comprehensive Cancer Center, 410 West Tenth Avenue, Room N-1022, Columbus, OH 43210
(NCI)W80-192	Woolley, P.V. 202-625-7081	Georgetown University Hospital, 3800 Reservoir Road, N.W., Washington, DC 20007
(NCI)W80-94	Young, C.W. 212-794-6672	Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10021

AT-125 (Acivicin)

NSC-163501

Protocol #	Principal Investigator	Address
(NCI)W80-194 WCCC-CO-8090	Davis, H. 608-263-8098	Wisconsin Clinical Cancer Center, University of Wisconsin, Department of Human Oncology, 600 Highland Avenue, Madison, WI 53792
(NCI)W80-302	Frei, E. 617-732-3555	Sidney Farber Cancer Institute, 35 Binney Street, Boston, MA 02115
(NCI)W79-204	Hoogstraten, B. 913-588-6029	University of Kansas Medical Center, Division of Clinical Oncology, 39th Street and Rainbow Boulevard, Kansas City, KS 66103
(NCI)W80-76	Ohnuma, T. 212-650-6664	Mount Sinai School of Medicine, Department of Neoplastic Diseases, 100th Street and Fifth Avenue, New York, NY 10029
(NCI)W80-237	Presant, C.A. 213-359-8111	City of Hope National Medical Center, Duarte, CA 91010

AZQ (Aziridinylbenzoquinone)

NSC-182986

Protocol #	Principal Investigator	Address
(NCI)W79-247 MDA-DT-7928	Bodey, G.P. 713-792-2121	M.D. Anderson Hospital and Tumor Institute, The University of Texas System Cancer Center, Houston, TX 77030
WSU-A-33580	Fraile, R.J. 313-577-1818	Wayne State University, Department of Oncology, 3990 John R Street, Detroit, MI 48201
(NCI)W79-180 PI-02-79	Hoogstraten, B. 913-588-6029	University of Kansas Medical Center, Division of Clinical Oncology, 39th Street and Rainbow Boulevard, Kansas City, KS 66103
(NCI)W79-208	Krakoff, I.H. 802-656-4414	Vermont Regional Cancer Center, University of Vermont, 1 South Prospect Street, Burlington, VT 05401
(NCI)N-8056 NCI-MB-137	Poplack, D.G.	National Cancer Institute, Division of Cancer Treatment, Bethesda, MD 20205
(NCI)W80-484	Siegel, S. 213-660-2450	Children's Hospital of Los Angeles, P.O. Box 54700, Terminal Annex, Los Angeles, CA 90054

Bromodeoxyuridine

NSC-38297

Protocol #	Principal Investigator	Address
NCI-80-C-143	Schwade, J.G.	National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Building 10, Room 6B15, Bethesda, MD 20205

DHAD (Dihydroxyanthracenedione)

NSC-301739

Protocol #	Principal Investigator	Address
(NCI)W79-281	Canellos, G. 617-732-3470	Sidney Farber Cancer Institute, 35 Binney Street, Boston, MA 02115
(NCI)W79-298	Cohen, L.E. 301-496-5007	National Cancer Institute, Pediatric Oncology Branch, Building 10, Room 3B06, Bethesda, MD 20205
(NCI)W79-278	Krakoff, I.H. 802-656-4414	Vermont Regional Cancer Center, University of Vermont, 1 South Prospect Street, Burlington, VT 05401
(NCI)W80-98	Neidhart, J.A. 614-422-5317	Ohio State University Comprehensive Cancer Center, 410 West Tenth Avenue, Room N-1022, Columbus, OH 43210
(NCI)W80-75	Ohnuma, T. 212-650-6664	Mount Sinai School of Medicine, Department of Neoplastic Diseases, 100th Street and Fifth Avenue, New York, NY 10029

DON (6-diazo-5-oxo-L-norleucine)

NSC-7365

Protocol #	**Principal Investigator**	**Address**
(NCI)W79-99	Davis, H.L. 608-263-8098	Wisconsin Clinical Cancer Center, University of Wisconsin, Department of Human Oncology, 600 Highland Avenue, Madison, WI 53792
(NCI)W79-242	Smith, F.P. 202-625-7706	Georgetown University Hospital, Department of Medical Oncology, Vincent T. Lombardi Cancer Research Center, Washington, DC 20007
(NCI)W80-565	Sullivan, M.P. 713-792-6624	M.D. Anderson Hospital, Pediatrics C6.035, Houston, TX 77030

ICRF-187

NSC-169780

Protocol #	**Principal Investigator**	**Address**
(NCI)W80-396	Vogel, C. 305-545-7707	Southeastern Cancer Study Group, Comprehensive Cancer Center, 1400 N.W. 10th Avenue, Center House Roof Garden, Miami, FL 33136

Indicine-N-oxide

NSC-132319

Protocol #	Principal Investigator	Address
(NCI)W80-455	Miser, J.	Children's Hospital Research Foundation, Ohio State University College of Medicine, Department of Pediatrics, Columbus Children's Hospital, 700 Children's Drive, Columbus, OH 43205

Methyl-GAG

NSC-32946

Protocol #	Principal Investigator	Address
MDAR-426 MDA-DT-8052	Bartologie, B. 713-792-2121	M.D. Anderson Hospital, Department of Developmental Therapeutics, The University of Texas System Cancer Center, Houston, TX 77030

VP-16213

NSC-141540

Protocol #	Principal Investigator	Address
BCRP-8019	Van Echo, D.A. 301-528-7912	Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 South Greene Street, Baltimore, MD 21201

2-DRUG COMBINATIONS

Adriamycin/ICRF-187

NSC-123127/NSC-169780

Protocol #	Principal Investigator	Address
(NCI)W80-310	Belt, R. 913-588-5996	University of Kansas Medical Center, 39th Street and Rainbow Boulevard, Kansas City, KS 66103

Ara-A (Vidarabine Phosphate)/Deoxycoformycin

NSC-247519/NSC-218321

Protocol #	Principal Investigator	Address
MDAR-427 MDA-DT-8060	Feun, L.G. 713-792-2121	M.D. Anderson Hospital, Department of Developmental Therapeutics, The University of Texas System Cancer Center, Houston, TX 77030

5-FU/PALA

NSC-19893/NSC-224131

Protocol #	Principal Investigator	Address
EST-PA-280	Camacho, F.J. 212-430-2015	Eastern Cooperative Oncology Group, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461

cis-Platinum/Thymidine

NSC-119875/NSC-21548

Protocol #	Principal Investigator	Address
MDAR-398	Valdivieso, M. 713-792-2121	University of Texas, M.D. Anderson Hospital & Tumor Institute, Houston, TX 77030

3-DRUG COMBINATIONS

5-FU/PALA/Thymidine

NSC-19893/NSC-224131/NSC-21548

Protocol #	Principal Investigator	Address
MDAR-397	Chiuten, D.F. 713-792-2121	University of Texas, M.D. Anderson Hospital & Tumor Institute, Houston, TX 22030
(NCI)W80-566	Young, C. 212-794-6672	Memorial Sloan Kettering Cancer Center, Developmental Chemotherapy Service, Solid Tumor Service, Department of Medicine, New York, NY 10021

MIXED MODALITIES

cis-Platinum/Radiation

NSC-119875

Protocol #	Principal Investigator	Address
EST-PB-380	Haselow, R.E. 612-725-6767	Eastern Cooperative Oncology Group, Veterans Administration Medical Center, Hematology Division, 54th Street and 48th Avenue South, Minneapolis, MN 55417

Melphalan/Cyclophosphamide/Bone Marrow Therapy

NSC-8806/NSC-26271

Protocol #	Principal Investigator	Address
MDAR-424 MDA/IM/8006	Bennetts, R.W. 713-792-2121	M.D. Anderson Hospital, Department of Medicine, The University of Texas System Cancer Center, Houston, TX 77030

SECTION 17

PROTOCOLS CLOSED IN 1980

BREAST TUMORS

CLB-7581 ADJUVANT CHEMOTHERAPY WITH CTX/MTX/5-FU, CTX/MTX/5-FU/VCR/PRED AND MER-BCG IMMUNOTHERAPY AFTER MASTECTOMY FOR BREAST CARCINOMA 17.0001
CLB-7682 PHASE III CHEMOTHERAPY WITH CTX/MTX/5-FU, CTX/5-FU/ADR, CTX/5-FU/ADR/VCR/PRED & MER-BCG IMMUNOTHERAPY FOR BREAST CARCINOMA . 17.0002
CLB-7881 PHASE III CHEMOTHERAPY WITH CAFVP VS CAFVP PLUS OOPHORECTOMY FOR METASTATIC BREAST CANCER IN PREMENOPAUSAL WOMEN 17.0003
SWOG-7725 PHASE III INDUCTION WITH VCR/5-FU/MTX/CTX/PRED PLUS MAINTENANCE WITH CMPF VS CMPF PLUS LEV IMMUNOTHERAPY FOR ER-BREAST CANCER . 17.0004
SWOG-7917 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE IN PREVIOUSLY TREATED PATIENTS WITH METASTATIC BREAST CARCINOMA 17.0005
MAYO-763204 MEGESTROL VS TAMOXIFEN FOR PERIMENOPAUSAL PATIENTS & DES VS TAMOXIFEN FOR POSTMENOPAUSAL PATIENTS WITH ADVANCED BREAST CANCER 17.0006
MAYO-773202 PHASE II CHEMOTHERAPY WITH MAYTANSINE OR CHLOROZOTOCIN FOR ADVANCED BREAST CANCER WITH CROSSOVER UPON PROGRESSION 17.0007
MDAR-229 ADJUVANT CHEMOTHERAPY WITH 5-FU/ADR/CTX WITH OR WITHOUT BCG IMMUNOTHERAPY AND RADIOTHERAPY FOR STAGE II OR III BREAST CARCINOMA 17.0008
MDAR-257 CONTINUOUS INFUSION CHEMOTHERAPY WITH ADRIAMYCIN FOR ADVANCED METASTATIC BREAST CANCER 17.0009
MDAR-272 PHASE II-III CHEMOTHERAPY WITH PEPTICHEMIO VS MELPHALAN IN REFRACTORY METASTATIC BREAST CANCER 17.0010
MDAR-275 IMMUNOTHERAPY WITH ALLOGENIC TUMOR VACCINE VS CULTURED TUMOR VACCINE FOR BREAST CANCER 17.0011
MDAR-283 PILOT CHEMOTHERAPY WITH ADR, DBD, AND MITOMYCIN-C FOR STAGE IV BREAST CANCER PATIENTS REFRACTORY TO CMF 17.0012
MDAR-306 PHASE II CHEMOTHERAPY WITH BRUCEANTIN FOR ADVANCED METASTATIC BREAST CANCER 17.0013
MDAR-311 PILOT PHASE I-II EVALUATION OF HUMAN FIBROBLAST INTERFERON FOR DISSEMINATED BREAST CANCER 17.0014
MDAR-314 PILOT CHEMOTHERAPY WITH CTX/ADR/PEPTICHEMIO INDUCTION, THIOTEPA/MTX/5-FU MAINTENANCE FOR METASTATIC BREAST CANCER 17.0015
MDAR-320 PILOT INDUCTION CHEMOTHERAPY WITH CTX/DBD/ADR AND MAINTENANCE WITH CTX/DBD/5-FU/MTX FOR METASTATIC BREAST CANCER 17.0016
MDAR-333 PHASE II CHEMOTHERAPY WITH AMSA AND ADRIAMYCIN FOR ADVANCED BREAST CANCER 17.0017

MDAR-352	PHASE II CHEMOTHERAPY WITH VBL/MTX PLUS CF RESCUE FOR REFRACTORY METASTATIC BREAST CANCER	17.0018
MDAR-354	PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED BREAST CANCER	17.0019
MDAR-359	PHASE II COMBINATION CHEMOTHERAPY WITH AMSA AND PEPTICHEMIO FOR METASTATIC BREAST CANCER	17.0020
MDAR-360	TWO-DRUG COMBINATION CHEMOTHERAPY WITH VINBLASTINE AND PEPTICHEMIO IN ADVANCED METASTATIC BREAST CANCER	17.0021
MDAR-364	PHASE II CHEMOTHERAPY WITH PCNU FOR STAGE IV BREAST CANCER REFRACTORY TO CONVENTIONAL CHEMOTHERAPY	17.0022
MDAR-410	PHASE II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR METASTATIC BREAST CANCER	17.0023
FRE-UNCHIM-02S75	ADJUVANT CHEMOTHERAPY WITH L-PAM VS VARIOUS COMBINATIONS OF VBL, CTX, THIOTEPA, STREPTONIGRIN, MTX, 5-FU, VCR AND PRED FOR BREAST CARCINOMA	17.0024
NZL-NBCG-1	ADJUVANT CHEMOTHERAPY WITH L-PAM WITH AND WITHOUT LEVAMISOLE IMMUNOTHERAPY AFTER SURGERY FOR BREAST CANCER WITH POSITIVE AXILLARY NODES	17.0025

GASTROINTESTINAL TUMORS

EST-3275	ADJUVANT STUDY WITH 5-FLUOROURACIL PLUS METHYL CCNU FOLLOWING CURATIVE GASTRIC RESECTION FOR ADENOCARCINOMA OF THE STOMACH	17.0026
GTSG-8174	ADJUVANT CHEMOTHERAPY WITH 5-FLUOROURACIL WITH OR WITHOUT METHYL CCNU FOLLOWING CURATIVE RESECTION FOR GASTRIC ADENOCARCINOMA	17.0027
VASOG-30	SURGICAL ADJUVANT COMBINATION CHEMOTHERAPY WITH 5-FU/MECCNU FOR CARCINOMA OF THE STOMACH	17.0028
SWOG-7738	PHASE III CHEMOTHERAPY WITH MITOMYCIN-C/5-FU WITH OR WITHOUT STREPTOZOTOCIN FOR PANCREATIC ADENOCARCINOMA	17.0029
CLB-7785	PREOPERATIVE RADIOTHERAPY FOR RECTAL ADENOCARCINOMA	17.0030
EST-1278	PHASE III 5-FU VS 5-FU/HU VS 5-FU/HU/MECCNU/DTIC VS MECCNU/DTIC VS MECCNU/ICRF VS MITO/DTIC FOR ADVANCED COLON AND RECTAL ADENOCARCINOMA	17.0031
SEG-78GI344	ADJUVANT RADIATION THERAPY AFTER CURATIVE RESECTION OF RECTAL CANCER, DUKES B2 AND C	17.0032
SEG-79GI268	PHASE II CHEMOTHERAPY WITH 5-FLUOROURACIL VS 6-THIOGUANINE FOR INCURABLE OR RESISTANT ADENOCARCINOMA OF THE COLON	17.0033
SWOG-7510	PHASE III CHEMOTHERAPY WITH 5-FU/MECCNU WITH OR WITHOUT ORAL BCG IMMUNOTHERAPY FOR LOCALLY ADVANCED ADENOCARCINOMA OF THE LARGE BOWEL	17.0034
GTSG-6178	ADJUVANT CHEMOTHERAPY WITH 5-FU BY PORTAL VEIN INFUSION FOR COLON ADENOCARCINOMA	17.0035
GTSG-7175	ADJUVANT RADIOTHERAPY AND CHEMOTHERAPY WITH 5-FU/MECCNU FOLLOWING CURATIVE RESECTION FOR RECTAL ADENOCARCINOMA	17.0036
MAYO-701872	ADJUVANT IMMUNOTHERAPY WITH MER-BCG DURING RADIOTHERAPY FOR PRIMARY ADENOCARCINOMA OF THE RECTUM	17.0037
MAYO-794601	PHASE II CHEMOTHERAPY WITH INDICINE-N-OXIDE FOR ADVANCED COLORECTAL CANCER	17.0038
MAYO-794605	PHASE II CHEMOTHERAPY WITH 6-THIOGUANINE FOR ADVANCED COLORECTAL ADENOCARCINOMA	17.0039
MDAR-276	FUDR/MITO HEPATIC ARTERY INFUSION WITH OR WITHOUT C. PARVUM IMMUNOTHERAPY FOR LIVER METASTASES OF COLORECTAL CANCER	17.0040
MDAR-343	PALA PLUS 5-FU INTRAVENOUS CHEMOTHERAPY GIVEN FOR 5 DAYS VS ONCE A WEEK FOR METASTATIC COLORECTAL CANCER	17.0041

MSKCC-7368 CHEMOTHERAPY WITH 5-FU/MECCNU AND/OR IMMUNOTHERAPY WITH MER ADJUVANT TO SURGERY FOR COLORECTAL ADENOCARCINOMA 17.0042
VASOG-27B IMMUNOTHERAPY WITH MER-BCG ADJUVANT TO CHEMOTHERAPY WTH 5-FU/MECCNU FOR RESIDUAL COLORECTAL CARCINOMA 17.0043
VASOG-33 ADJUVANT CHEMOTHERAPY WITH 5-FU VS 5-FU/HU FOR MALE PATIENTS FOLLOWING SURGERY FOR COLON OR RECTAL CANCER 17.0044
FRE-UNCHIM-01CG76 POSTSURGICAL CHEMOTHERAPY WITH 5-FU VS VBL/THIOTEPA/STREPTONIGRIN/5-FU FOR COLORECTAL CARCINOMA, MODIFIED DUKES A, B, C1 OR C2 .... 17.0045
UICC-76126 SINGLE VS MULTIPLE FRACTION RADIOTHERAPY FOLLOWED BY SURGERY FOR ADENOCARCINOMA OF THE RECTUM 17.0046
UKM-OXF-8082 INTERMITTENT ADJUVANT IMMUNOTHERAPY WITH C. PARVUM FOLLOWING SURGERY FOR COLORECTAL CANCER 17.0047
EST-1274 RADIOTHERAPY AND 5-FLUOROURACIL CHEMOTHERAPY FOR LOCALLY UNRESECTABLE STOMACH, PANCREATIC, RECTAL AND BILIARY TRACT CANCER 17.0048
SEG-77GI0202 PHASE II CHEMOTHERAPY WITH CYCLIC DAILY ANGUIDINE FOR GASTROINTESTINAL TRACT ADENOCARCINOMA 17.0049
SEG-78GI0102 PHASE I-II CHEMOTHERAPY WITH ICRF-159/ADRIAMYCIN FOR ADVANCED METASTATIC ADENOCARCINOMA OF THE GASTROINTESTINAL TRACT 17.0050
SEG-79GI260 PHASE II CHEMOTHERAPY WITH M-AMSA FOR FAR ADVANCED GASTROINTESTINAL CANCER 17.0051
MAYO-790308/794801 PILOT AND PHASE II COMBINED CHEMOTHERAPY WITH FAP (ADR/CACP/5-FU) FOR ADVANCED GASTRIC AND PANCREATIC CARCINOMA 17.0052
MDAR-296 COMBINATION CHEMOTHERAPY WITH 5-FLUOROURACIL, VINDESINE, AND METHYL CCNU FOR METASTATIC GASTROINTESTINAL MALIGNANCIES 17.0053

GENITOURINARY TUMORS

RTOG-7821 PHASE I/II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS RADIOTHERAPY FOR BLADDER CANCER 17.0054
EST-3877 VBL/CCNU, TZT, OR ACT-D, PALA, AMSA OR INDICINE CHEMOTHERAPY AND MASTER PHASE II PROTOCOL FOR ADVANCED RENAL CELL CANCER 17.0055
SWOG-7805 INDUCTION AND MAINTENANCE CHEMOTHERAPY WITH YOSHI 864 PLUS HORMONE THERAPY WITH MPA FOR ADENOCARCINOMA OF THE KIDNEY IN ADULTS 17.0056
EST-PB-878 PHASE II PILOT CHEMOTHERAPY WITH TAMOXIFEN FOR ADVANCED CARCINOMA OF THE PROSTATE 17.0057
NPCP-500 CHEMOTHERAPY WITH CTX PLUS HORMONE THERAPY WITH ESTRACYT OR DES VS DES ALONE OR ORCHIECTOMY ALONE FOR STAGE D PROSTATIC CARCINOMA 17.0058
SEG-78GU232 HORMONE THERAPY WITH TAMOXIFEN FOR PROSTATIC CARCINOMA 17.0059
IL-PR-2 HORMONE THERAPY WITH DIETHYLSTILBESTROL PLUS IMMUNOTHERAPY WITH LEVAMISOLE IN STAGE D PROSTATE CANCER 17.0060
EST-1877 VAB III (CTX/ACT-D/VBL/BLEO) WITH HIGH VS LOW DOSE CACP FOLLOWED BY VAP OR AVP/CAP/VAP MAINTENANCE FOR TESTICULAR TUMORS 17.0061
MSKCC-7712 CHEMOTHERAPY WITH CTX, VBL, ACT-D, BLEO, CACP, ADR FOR UNRESECTABLE STAGE II AND STAGE III NONSEMINOMATOUS GERM-CELL TUMORS 17.0062

GYNECOLOGIC TUMORS

EST-PE-878 PILOT IMMUNOTHERAPY WITH INTRAPERITONEAL BCG PLUS MELPHALAN/ISONIAZID CHEMOTHERAPY FOR STAGE IC, II OR III OVARIAN ADENOCARCINOMA 17.0063
EST-2878 PHASE III CHEMOTHERAPY WITH L-PAM FOLLOWED BY HAD (HMM/ADR/CACP) VS CHAD (CTX/ADR/HMM/CACP) FOR ADVANCED ADENOCARCINOMA OF THE OVARY 17.0064

GOG-12 PHASE II COMBINATION CHEMOTHERAPY WITH ACT-D/MTX/CLB FOR OVARIAN GERM CELL TUMORS CONTAINING CHORIOCARCINOMA 17.0065

GOG-13 PHASE II CHEMOTHERAPY WITH ACT-D/VCR PLUS RADIOTHERAPY FOLLOWED BY CTX/ACT-D FOR MIXED MESODERMAL OVARIAN TUMORS 17.0066

BCRP-7827 CHEMOTHERAPY WITH ADR PLUS VP-16 FOR STAGE III/IV ADENOCARCINOMA OF THE OVARY 17.0067

GOG-P12 RELATION OF PROGESTIN RECEPTOR CONCENTRATION TO EFFICACY OF PROGESTIN THERAPY FOR ENDOMETRIAL ADENOCARCINOMA - PILOT STUDY 17.0068

GOG-7892 PHASE II HORMONE THERAPY WITH TAMOXIFEN FOR ADVANCED OR RECURRENT ENDOMETRIAL ADENOCARCINOMA 17.0069

CAN-NCIC-TO-1 CHEMOTHERAPY WITH 5-FU AND MEDROXYPROGESTERONE ACETATE AND WITH MELPHALAN FOR ADVANCED ENDOMETRIAL CARCINOMA 17.0070

SWOG-7524 PHASE II CHEMOTHERAPY WITH ADR/CTX WITH AND WITHOUT BCG IMMUNOTHERAPY FOR OVARIAN AND ENDOMETRIAL CARCINOMA, STAGES III AND IV 17.0071

MYELOMA AND OTHER HEMATOLOGIC TUMORS

CLB-7801 PILOT PHASE II STUDY OF CHLOROZOTOCIN FOR MULTIPLE MYELOMA 17.0072

MDAR-388 PHASE I-II IMMUNOTHERAPY WITH POLY ICLC FOR MULTIPLE MYELOMA 17.0073

CCG-981 PHASE II SEQUENTIAL HEMI-BODY RADIOTHERAPY FOR RECURRENT HISTIOCYTOSIS X IN CHILDREN 17.0074

PVSG-14 CHEMOTHERAPY WITH CIMETIDINE FOR PRURITUS DUE TO POLYCYTHEMIA VERA 17.0075

LEUKEMIA

CLB-7612 PHASE III VCR/L-ASP/PRED & DNM INDUCTION, 6-MP/MTX/VCR/PRED MAINTENANCE & MER-BCG FOR ACUTE LYMPHOCYTIC LEUKEMIA 17.0076

CLB-7901 PILOT INTENSIVE MTX/CF CONSOLIDATION THERAPY WITH PROTOCOL CLB-7611 INDUCTION AND MAINTENANCE FOR HIGH-RISK ALL IN CHILDREN 17.0077

NCI-79-C-103 PHASE I STUDY OF 2 PRIME-DEOXYCOFORMYCIN IN ACUTE LYMPHOBLASTIC LEUKEMIA 17.0078

SJCRH-ALL-TT-9 VCR/DNM/PRED INDUCTION WITH OR WITHOUT L-ASP, ARA-C, CNS RADIOTHERAPY PLUS MTX, AND MAINTENANCE WITH 6-MP/MTX FOR CHILDREN WITH ALL 17.0079

INA-TAT-TMC1 COMBINATION CHEMOTHERAPY WITH VCR/PRDL WITH OR WITHOUT REINFORCEMENT AND 6-MP/MTX FOR NON-T CELL ACUTE LYMPHOCYTIC LEUKEMIA IN CHILDREN 17.0080

MDAR-336 COMBINATION CHEMOTHERAPY WITH ROAP (RBD/ARA-C/VCR/PRED), POMP (6-MP/MTX/VCR/PRED) AND OAP (ARA-C/VCR/PRED) PLUS TG WITH OR WITHOUT MER FOR AML 17.0081

RPMI-DMA-970701 ALLOGENEIC TUMOR CELLS DURING INTENSIVE MAINTENANCE CHEMOTHERAPHY AFTER INDUCTION WITH ARA-C/ADR FOR ACUTE MYELOCYTIC LEUKEMIA 17.0082

SJCRH-AML-76 CHEMOTHERAPY WITH VCR, DNM, ARA-C, AZUR, MTX, L-ASP, ADR, CTX AND 6-MP WITH OR WITHOUT SPLENECTOMY FOR ACUTE NONLYMPHOCYTIC LEUKEMIA 17.0083

JAP-ANLL-N-CWS-1 MAINTENANCE CHEMOTHERAPY WITH DNM, ARA-C, 6-MP, PRDL, VCR, CTX WITH AND WITHOUT NOCARDIA RUBRA CWS AND ALLOGENEIC LEUKEMIA CELLS IN ANLL 17.0084

EST-3476 PHASE III CHEMOTHERAPY WITH CLB/PRED AND CTX/ARA-C/PRED VS TOTAL BODY RADIOTHERAPY FOR CHRONIC LYMPHOCYTIC LEUKEMIA 17.0085

SWOG-7831 PHASE II CHEMOTHERAPY WITH NEOCARZINOSTATIN FOR ACUTE LYMPHOCYTIC OR ACUTE NONLYMPHOCYTIC LEUKEMIA IN CHILDREN 17.0086

LUNG TUMORS

EST-PB-579	PILOT STUDY CHEMOTHERAPY WITH CCM INDUCTION AND RADIOTHERAPY CONSOLIDATION OF SMALL CELL UNDIFFERENTIATED LUNG CARCINOMA	17.0087
SEG-LUN-P31	PHASE I-II CHEMOTHERAPY WITH VP-16/CCNU/PROCARBAZINE FOR DISSEMINATED SMALL CELL CARCINOMA OF THE LUNG	17.0088
SEG-80LUN271	PHASE II CHEMOTHERAPY WITH ACRIDINYL ANISIDIDE (M-AMSA) FOR ADVANCED SMALL CELL CARCINOMA OF THE LUNG	17.0089
MDAR-235	MEGADOSE CHEMOTHERAPY WITH VCR/CTX/VP-16/BCNU WITH AUTOLOGOUS BONE MARROW RESCUE FOR OAT CELL CARCINOMA OF THE LUNG	17.0090
MDAR-267	CHEMOTHERAPY IN PEPA WITH ECHO (VP-16/CTX/ADR/VCR) PLUS PRIME (PCB/IPP/MTX) PLUS RADIOTHERAPY FOR SMALL CELL LUNG CANCER	17.0091
MDAR-290	VP-16/CTX/ADR/VCR AND PCB/IPP/MTX WITH OR WITHOUT INTRAVENOUS HYPERALIMENTATION FOR SMALL CELL BRONCHOGENIC CARCINOMA	17.0092
MSKCC-7891	CTX/ADR/VCR INDUCTION WITH ADDED CCNU/MTX/PCB OR CTX/VCR PLUS RADIOTHERAPY CONSOLIDATION FOR SMALL CELL LUNG CANCER	17.0093
TN-LUN-L38	CHEMOTHERAPY WITH MTX VS MTX PLUS IMMUNOTHERAPY IN LIMITED STAGE SMALL CELL LUNG CANCER WITH PRIOR COMBINATION CHEMO AND RADIATION THERAPY	17.0094
EST-PD-578	RADIOTHERAPY PLUS HAM (HMM/ADR/MTX) CHEMOTHERAPY FOR NONRESECTABLE NON-OAT-CELL LUNG CANCER	17.0095
EST-1579	PHASE II MASTER PROTOCOL AND TRIALS WITH AMSA AND NEOCARZINOSTATIN FOR NON-SMALL CELL LUNG CARCINOMA	17.0096
RTOG-7814	PHASE I/II STUDY OF HYPOXIC CELL SENSITIZER MISONIDAZOLE PLUS RADIOTHERAPY FOR LOCALLY ADVANCED LUNG CARCINOMA	17.0097
SWOG-7807	PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR REFRACTORY EPIDERMOID CARCINOMA OF THE LUNG	17.0098
SWOG-7971	PHASE II/PILOT COMBINATION CHEMOTHERAPY WITH MITO/DAVA/5-FU FOR ADENOCARCINOMA AND LARGE CELL CARCINOMA OF THE LUNG	17.0099
SWOG-8003	PHASE II EVALUATION OF ME-GAG IN THE TREATMENT OF INCURABLE, ADVANCED, METASTATIC NON-OAT CELL CARCINOMA OF THE LUNG	17.0100
LCSG-771	ADJUVANT IMMUNOTHERAPY WITH POSTOPERATIVE INTRAPLEURAL BCG FOR LUNG CARCINOMA	17.0101
MAYO-772203	PHASE II CHEMOTHERAPY WITH DAP-II (DAG/ADR/CACP) FOLLOWED BY CTX/VP-16 FOR ADVANCED SQUAMOUS CELL LUNG CANCER	17.0102
MAYO-782301	VP-16/CYCLOPHOSPHAMIDE/ADRIAMYCIN/CIS-PLATINUM FOR ADVANCED LARGE CELL LUNG CANCER	17.0103
MAYO-782502	PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED LUNG CANCER	17.0104
MAYO-792402	PHASE II CHEMOTHERAPY WITH INTERMITTENT DIBROMODULCITOL FOR ADVANCED NON-SMALL CELL LUNG CANCER	17.0105
MDAR-286	PHASE II CHEMOTHERAPY WITH AMSA FOR METASTATIC LUNG CANCER REFRACTORY TO PRIMARY THERAPY	17.0106
MDAR-318	VAP (DAVA/ADR/CACP) CHEMOTHERAPY WITH/WITHOUT THYMOSIN FOR METASTATIC DISSEMINATED NON-OAT CELL LUNG CARCINOMA	17.0107
MSKCC-786	COMBINATION CHEMOTHERAPY WITH HIGH VS LOW DOSE CIS-PLATINUM/VINDESINE FOR NON SMALL CELL LUNG CANCER	17.0108
MSKCC-7942	COMBINATION CHEMOTHERAPY WITH CACP/ADR/CTX/DAVA VS CACP/CTX/DAVA FOR UNRESECTABLE OR METASTATIC NON-SMALL CELL LUNG CANCER	17.0109
NCI-79-C-37	PHASE II CHEMOTHERAPY WITH ADR/MITO IN ADVANCED NON-SMALL CELL CARCINOMA OF THE LUNG	17.0110
VASOG-34A	INTRAPLEURAL VS INTRADERMAL BCG FOR NON-SMALL CELL CARCINOMA OF THE LUNG WITHOUT LYMPHNODE METASTASES	17.0111
VASOG-34B	POSTSURGICAL RADIOTHERAPY FOR RESECTED NON-SMALL CELL CARCINOMA OF THE LUNG WITH LYMPHNODE METASTASES	17.0112

JAP-LC-N-CWS PHASE III IMMUNOTHERAPY WITH NOCARDIA RUBRA CELL WALL SKELETON FOR LUNG CANCER 17.0113
JAP-PL-N-CWS ADJUVANT IMMUNOTHERAPY WITH NOCARDIA RUBRA CELL WALL SKELETON (N-CWS) AFTER INDUCTION CHEMOTHERAPY WITH MITOMYCIN-C FOR LUNG CANCER 17.0114
UKM-OXF-8081 SPECIFIC IMMUNOTHERAPY WITH IRRADIATED AUTOLOGOUS TUMOR CELLS AND CORYNEBACTERIUM PARVUM FOR RESECTABLE LUNG CANCER 17.0115

LYMPHOMA

SWOG-7518 RADIOTHERAPY PLUS CHEMOTHERAPY WITH NM/VCR/PCB/PRED/BLEO VS CHEMOTHERAPY FOR STAGE III A & B HODGKIN'S DISEASE - A PHASE III STUDY 17.0116
CAN-NCIC-HD3 MOPP CHEMOTHERAPY WITH OR WITHOUT ABVD WITH LOW OR HIGH DOSE RADIOTHERAPY FOR STAGE III AND IV HODGKIN'S DISEASE 17.0117
SJCRH-NHL-75 MULTIMODALITY THERAPY FOR THE INDUCTION, CNS PROPHYLAXIS AND MAINTENANCE OF NON-HODGKIN'S LYMPHOMA 17.0118
VEN-NHL-1 ADR, ARA-C, BLEO, CLB, CTX, PRED, TG, VCR COMBINATION CHEMOTHERAPY WITH AND WITHOUT RADIOTHERAPY & HORMONE THERAPY IN NON-HODGKIN'S LYMPHOMA 17.0119
EST-1478 PHASE II MASTER PROTOCOL AND CHEMOTHERAPY WITH VM-26/PRED PLUS CIS-PLATINUM OR HEXAMETHYLMELAMINE FOR LYMPHOMA 17.0120
SWOG-7821 PHASE II CHEMOTHERAPY WITH MAYTANSINE FOR ADVANCED HODGKIN'S AND NON-HODGKIN'S LYMPHOMA 17.0121
BCRP-7101A MULTIPLE MODALITY TREATMENT FOR LYMPHOSARCOMA AND RETICULUM CELL SARCOMA 17.0122

MELANOMA AND OTHER SKIN CANCERS

EST-PC-678 PHASE II PILOT STUDY WITH AMSA FOR METASTATIC MALIGNANT MELANOMA 17.0123
RTOG-7919 PHASE II CHEMOTHERAPY WITH BLEO, CACP, OR BCNU WITH/WITHOUT HYPERTHERMIA FOR SUPERFICIAL LESIONS 17.0124
SEG-360 PHASE III STUDY OF ADJUVANT IMMUNOTHERAPY WITH CORYNEBACTERIUM PARVUM VACCINE FOR STAGE II MELANOMA 17.0125
SWOG-7874 PHASE II EVALUATION OF TAMOXIFEN IN PATIENTS WITH RECURRENT MALIGNANT MELANOMA 17.0126
MAYO-787003 PHASE II CHEMOTHERAPY WITH PALA AND/OR AMSA FOR ADVANCED MALIGNANT MELANOMA 17.0127
MDAR-317 PHASE II CHEMOTHERAPY WITH AMSA WITH OR WITHOUT DTIC FOR METASTATIC MALIGNANT MELANOMA 17.0128
NCI-77-C-151 DEEP INGUINAL LYMPH NODE DISSECTION FOR MALIGNANT MELANOMA WITH POSITIVE SUPERFICIAL INGUINAL NODES 17.0129
NCI-77-C-154 IMMUNOTHERAPY WITH DINITROCHLOROBENZENE FOR MULTIPLE SKIN TUMORS 17.0130
NCI-78-C-79 TOPICAL IMMUNOTHERAPY OF CUTANEOUS MALIGNANCIES WITH CONTACT SENSITIZERS 17.0131
CAN-CCI-MEL-1 ADJUVANT IMMUNOTHERAPY WITH BCG IN STAGE I MALIGNANT MELANOMA 17.0132
FRE-UNCHIM-4NK76 DTIC/VBL/THIOTEPA/MTX/STREPTONIGRIN/PROCARBAZINE WITH OR WITHOUT BCG/C. PARVUM FOR MELANOMA 17.0133
UICC-73052 ADJUVANT CHEMOTHERAPY AND IMMUNOTHERAPY FOR RESECTED CUTANEOUS MELANOMA WITH OR WITHOUT REGIONAL LYMPH-NODE METASTASES 17.0134
UICC-76016 CHEMOTHERAPY WITH DTIC PLUS IMMUNOTHERAPY WITH BCG OR C. PARVUM FOR ADVANCED AND METASTATIC MELANOMA 17.0135

SARCOMA

CLB-7583 ADJUVANT CHEMOTHERAPY WITH ADR VS. ADR/MTX/CF VS. ADR/CTX FOLLOWING SURGERY FOR OSTEOGENIC SARCOMA 17.0136
RTOG-7402 OPTIMAL FRACTIONATION SCHEDULE OF PALLIATIVE RADIOTHERAPY FOR RELIEF OF PAIN DUE TO OSSEOUS METASTASES 17.0137
NCI-78-C-64 PHASE II CHEMOTHERAPY WITH 5-AZACYTIDINE FOR REFRACTORY OSTEOGENIC SARCOMA AND EWING'S SARCOMA 17.0138
CAN-NCIC-7702 CIS-PLATINUM FOR REFRACTORY UNRESECTABLE OSTEOSARCOMA 17.0139
CAN-UICC-76001 CONCURRENT VS SEQUENTIAL COMBINATION CHEMOTHERAPY WITH ADR/MTX/CF FOR OSTEOGENIC SARCOMA 17.0140
SWOG-7802 PHASE III ADJUVANT RADIOTHERAPY WITH AND WITHOUT CHEMOTHERAPY WITH DTIC/ADRIAMYCIN FOR SOFT TISSUE SARCOMA 17.0141
EORTC-62792 PHASE II CHEMOTHERAPY WITH LOW-DOSE METHOTREXATE FOR REFRACTORY SOFT TISSUE SARCOMA 17.0142
SEG-77SAR0103 PHASE III ADJUVANT STUDY OF IMMUNOTHERAPY WITH C. PARVUM AND CHEMOTHERAPY WITH CAM (CTX/ADR/MTX) IN SOFT TISSUE AND BONE SARCOMAS 17.0143
SWOG-7911 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE FOR INCURABLE ADVANCED SOFT TISSUE AND BONE SARCOMAS 17.0144

PEDIATRIC SOLID TUMORS

UICC-76068 PREOPERATIVE AND POSTOPERATIVE RADIOTHERAPY AND CHEMOTHERAPY WITH ACT-D/VCR FOR WILMS' TUMOR 17.0145
CCG-371P/373P PHASE III PILOT STUDY WITH CTX/VCR/DTIC FOLLOWED BY CTX/ADR ALTERNATING WITH VM-26 FOR STAGE III AND IV CHILDHOOD NEUROBLASTOMA 17.0146
CCG-075 PHASE II CHEMOTHERAPY WITH AZAPICYL FOR RHABDOMYOSARCOMA AND UNDIFFERENTIATED SARCOMA IN CHILDREN 17.0147
SWOG-7898 CHEMOTHERAPY WITH VAC (VCR/ACT-D/CTX) AND VADRC (VCR/ADR/CTX) PLUS RADIOTHERAPY AND/OR SURGERY FOR PRIMARY PELVIC RHABDOMYOSARCOMA 17.0148
SWOG-7896 HIGH VS MODERATE DOSE CHEMOTHERAPY WITH VCR/ADR/CTX/ACT-D PLUS RADIOTHERAPY FOLLOWING SURGERY FOR PRIMARY EWING'S SARCOMA OF BONE 17.0149
CCG-071 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR CHILDREN WITH VARIOUS ADVANCED SOLID TUMORS 17.0150
CCG-961 ADJUVANT PHASE III CHEMOTHERAPY WITH CTX/VCR FOR CHILDHOOD LOCALIZED UNILATERAL RETINOBLASTOMA 17.0151
CCG-962 PHASE III CHEMOTHERAPY WITH CTX/VCR OR CTX/VCR/ADR/MTX PLUS RADIOTHERAPY FOR EXTRAOCULAR RETINOBLASTOMA 17.0152

HEAD AND NECK TUMORS

EST-1375 ADJUVANT CHEMOTHERAPY WITH MTX AND IMMUNOTHERAPY WITH C. PARVUM FOR STAGE III-IV SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK 17.0153
EST-1377 PHASE III THERAPY WITH MTX WITH OR WITHOUT C. PARVUM OR BLEO/CACP FOR ADVANCED SQUAMOUS CELL CANCER OF THE HEAD AND NECK 17.0154
RTOG-7619 REGISTRY OF HEAD AND NECK TUMORS TREATED WITH RADIOTHERAPY ALONE OR IN COMBINATION WITH SURGERY AND/OR CHEMOTHERAPY 17.0155
MAYO-777401 PHASE II CHEMOTHERAPY WITH CTX/ADR/CACP FOLLOWED UPON FAILURE BY MAYTANSINE FOR ADVANCED HEAD AND NECK CANCER 17.0156
MAYO-787402 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED HEAD AND NECK CANCER 17.0157

UICC-76003 MTX VS MTX ALTERNATING WITH VBL/BLEO CHEMOTHERAPY FOLLOWING CURATIVE RADIOTHERAPY FOR LOCALLY ADVANCED CARCINOMA OF THE OROPHARYNX 17.0158

BRAIN AND OTHER CNS TUMORS

CCG-944 PHASE III COMBINATION CHEMOTHERAPY WITH VCR/CCNU/PRED VS PCB & RADIOTHERAPY FOR BRAIN STEM TUMORS IN CHILDREN 17.0159

RTOG-7823 PHASE I-II MISONIDAZOLE RADIOSENSITIZATION PRIOR TO RADIOTHERAPY FOR RECURRENT BRAIN TUMORS IN CHILDREN 17.0160

CAN-UICC-76103 COMBINATION CHEMOTHERAPY WITH CCNU/HU AND RADIOTHERAPY FOR ASTROCYTOMA GRADES III AND IV 17.0161

EORTC-26782 PHASE II COMBINATION CHEMOTHERAPY WITH LOW-DOSE DDMP/CITROVORUM FACTOR FOR RECURRENT BRAIN GLIOMAS 17.0162

URU-CNS-64 VM-26 CHEMOTHERAPY FOR TUMORS OF THE CENTRAL NERVOUS SYSTEM 17.0163

UNSPECIFIED OR MULTIPLE NEOPLASMS

CLB-0704 PHASE II CHEMOTHERAPY WITH NEOCARZINOSTATIN FOR ACUTE LEUKEMIA AND FOR VARIOUS SOLID TUMORS 17.0164

CLB-7701 PILOT-PHASE II CHEMOTHERAPY WITH INOX FOR ADVANCED TESTICULAR CANCER, MELANOMA, OAT CELL CARCINOMA, AND SARCOMA 17.0165

RTOG-7710 PHASE I-II STUDY OF RADIOTHERAPY AND/OR HYPERTHERMIA FOR SUPERFICIAL HUMAN TUMORS 17.0166

RTOG-7816 PHASE I-II HYPERTHERMIA (43.5 DEGREES CENTIGRADE) BEFORE AND AFTER RADIATION TREATMENT FOR HUMAN TUMORS 17.0167

SEG-267R PHASE II HMM THERAPY FOR HODGKIN'S & NON-HODGKIN'S LYMPHOMA, CHRONIC LYMPHOCYTIC LEUKEMIA, AND CARCINOMA OF THE OVARY & CERVIX 17.0168

SWOG-7860 PHASE II PILOT CHEMOTHERAPY WITH METHYL-GAG FOR SOLID TUMORS AND REFRACTORY HEMATOLOGIC MALIGNANCIES 17.0169

MDAR-228 PHASE II CHEMOTHERAPY WITH NZS FOR CHRONIC AND ACUTE LEUKEMIAS, LYMPHOMA, AND LIVER, RENAL, AND BLADDER CARCINOMAS 17.0170

MSKCC-65163 IMMUNOTHERAPY WITH TRANSFER FACTOR FOR MEASURABLE CANCER 17.0171

MSKCC-717 IMMUNOTHERAPY WITH IRRADIATED AUTOLOGOUS CANCER CELLS AND BCG FOR NONRESECTABLE CANCER 17.0172

MSKCC-7629 CHEMOTHERAPY WITH HIGH-DOSE CACP AND MANNITOL DIURESIS FOR ADVANCED CANCER 17.0173

GA-EU-1-CB-64061 STUDIES OF IMMUNOLOGICAL STIMULANTS IN PATIENTS RECEIVING RADIATION THERAPY FOR CARCINOMA OF HEAD AND NECK, UTERINE CERVIX AND LUNG 17.0174

SJCRH-PODOPH-1 CHEMOTHERAPY WITH VM-26 OR VP-16 IN CHILDREN WITH ACUTE LEUKEMIA OR SOLID TUMORS 17.0175

SECTION 17

PROTOCOLS CLOSED IN 1980

BREAST TUMORS

17.0001 ADJUVANT CHEMOTHERAPY WITH CTX/MTX/5-FU, CTX/MTX/5-FU/VCR/PRED AND MER-BCG IMMUNOTHERAPY AFTER MASTECTOMY FOR BREAST CARCINOMA

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-7581
CLOSING DATE: 10/80
PATIENT ACCRUAL: 05581078

17.0002 PHASE III CHEMOTHERAPY WITH CTX/MTX/5-FU, CTX/5-FU/ADR, CTX/5-FU/ADR/VCR/PRED & MER-BCG IMMUNOTHERAPY FOR BREAST CARCINOMA

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-7682
CLOSING DATE: 02/80
PATIENT ACCRUAL: 02831078

17.0003 PHASE III CHEMOTHERAPY WITH CAFVP VS CAFVP PLUS OOPHORECTOMY FOR METASTATIC BREAST CANCER IN PREMENOPAUSAL WOMEN

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-7881
CLOSING DATE: 04/80

17.0004 PHASE III INDUCTION WITH VCR/5-FU/MTX/CTX/PRED PLUS MAINTENANCE WITH CMPF VS CMPF PLUS LEV IMMUNOTHERAPY FOR ER-BREAST CANCER

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7725
CLOSING DATE: 07/80
PATIENT ACCRUAL: 01120279

17.0005 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE IN PREVIOUSLY TREATED PATIENTS WITH METASTATIC BREAST CARCINOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7917
CLOSING DATE: 07/80

17.0006 MEGESTROL VS TAMOXIFEN FOR PERIMENOPAUSAL PATIENTS & DES VS TAMOXIFEN FOR POSTMENOPAUSAL PATIENTS WITH ADVANCED BREAST CANCER

Ingle, J. N., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-763204
CLOSING DATE: 06/80
PATIENT ACCRUAL: 01390279

17.0007 PHASE II CHEMOTHERAPY WITH MAYTANSINE OR CHLOROZOTOCIN FOR ADVANCED BREAST CANCER WITH CROSSOVER UPON PROGRESSION

Edmonson, J. H., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-773202
CLOSING DATE: 05/80
TERMINATION DATE: 06/80
PATIENT ACCRUAL: 00210279

17.0008 ADJUVANT CHEMOTHERAPY WITH 5-FU/ADR/CTX WITH OR WITHOUT BCG IMMUNOTHERAPY AND RADIOTHERAPY FOR STAGE II OR III BREAST CARCINOMA

Buzdar, A. U., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-229; MDA-DT-7730
CLOSING DATE: 09/80

17.0009 CONTINUOUS INFUSION CHEMOTHERAPY WITH ADRIAMYCIN FOR ADVANCED METASTATIC BREAST CANCER

Legha, S. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-257; MDA-MBDT-7774
CLOSING DATE: 09/80

17.0010 PHASE II-III CHEMOTHERAPY WITH PEPTICHEMIO VS MELPHALAN IN REFRACTORY METASTATIC BREAST CANCER

Buzdar, A. U., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-272; MDA-MBDT-7814
CLOSING DATE: 09/80
PATIENT ACCRUAL: 00640979

PROTOCOLS CLOSED IN 1980—Complete summaries available in CLINPROT data base

17.0011 IMMUNOTHERAPY WITH ALLOGENIC TUMOR VACCINE VS CULTURED TUMOR VACCINE FOR BREAST CANCER

Wiseman, C. L., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-275; MDA-DT-7817
CLOSING DATE: 09/80

17.0012 PILOT CHEMOTHERAPY WITH ADR, DBD, AND MITOMYCIN-C FOR STAGE IV BREAST CANCER PATIENTS REFRACTORY TO CMF

DiStefano, A., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-283; MDA-MBDT-7825
CLOSING DATE: 09/80

17.0013 PHASE II CHEMOTHERAPY WITH BRUCEANTIN FOR ADVANCED METASTATIC BREAST CANCER

Wiseman, C. L., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-306; MDA-MBDT-7846
CLOSING DATE: 09/80

17.0014 PILOT PHASE I-II EVALUATION OF HUMAN FIBROBLAST INTERFERON FOR DISSEMINATED BREAST CANCER

Gutterman, J. U., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-311; MDA-MBDT-7866
CLOSING DATE: 09/80

17.0015 PILOT CHEMOTHERAPY WITH CTX/ADR/PEPTICHEMIO INDUCTION, THIOTEPA/MTX/5-FU MAINTENANCE FOR METASTATIC BREAST CANCER

Legha, S. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-314; MDA-MBDT-7855
CLOSING DATE: 09/80

17.0016 PILOT INDUCTION CHEMOTHERAPY WITH CTX/DBD/ADR AND MAINTENANCE WITH CTX/DBD/5-FU/MTX FOR METASTATIC BREAST CANCER

DiStefano, A., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-320; MDA-DT-7863
CLOSING DATE: 09/80

17.0017 PHASE II CHEMOTHERAPY WITH AMSA AND ADRIAMYCIN FOR ADVANCED BREAST CANCER

Legha, S. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Institute, Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-333; MDA-MBDT-7922
CLOSING DATE: 09/80

17.0018 PHASE II CHEMOTHERAPY WITH VBL/MTX PLUS CF RESCUE FOR REFRACTORY METASTATIC BREAST CANCER

Hortobagyi, G. N., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-352; MDA-MBDT-7936
CLOSING DATE: 09/80

17.0019 PHASE II CHEMOTHERAPY WITH METHYL-GAG FOR ADVANCED BREAST CANCER

Yap, H. Y., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-354; MDA-MBDT-7932
CLOSING DATE: 09/80

17.0020 PHASE II COMBINATION CHEMOTHERAPY WITH AMSA AND PEPTICHEMIO FOR METASTATIC BREAST CANCER

Buzdar, A. U., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-359; MDA-MBDT-7944
CLOSING DATE: 09/80

17.0021 TWO-DRUG COMBINATION CHEMOTHERAPY WITH VINBLASTINE AND PEPTICHEMIO IN ADVANCED METASTATIC BREAST CANCER

Yap, H. Y., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-360; MDA-MBDT-7934
CLOSING DATE: 09/80

17.0022 PHASE II CHEMOTHERAPY WITH PCNU FOR STAGE IV BREAST CANCER REFRACTORY TO CONVENTIONAL CHEMOTHERAPY

Yap, H. Y., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-364; MDA-MBDT-7961
CLOSING DATE: 09/80

17.0023 PHASE II CHEMOTHERAPY WITH ANTHRACENEDIONE FOR METASTATIC BREAST CANCER

Yap, H. Y., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-410; MDA-MBDT-8037
CLOSING DATE: 10/80

17.0024 ADJUVANT CHEMOTHERAPY WITH L-PAM VS VARIOUS COMBINATIONS OF VBL, CTX, THIOTEPA, STREPTONIGRIN, MTX, 5-FU, VCR AND PRED FOR BREAST CARCINOMA

Jacquillat, C., (Paris 200.08.46) Hopital St. Louis, Chemotherapy Unit, 2 Pl. du Docteur Fournier, 75475 Paris 10, France
PROTOCOL NUMBER(S) FRE-UNCHIM-02S75
CLOSING DATE: 05/80

17.0025 ADJUVANT CHEMOTHERAPY WITH L-PAM WITH AND WITHOUT LEVAMISOLE IMMUNOTHERAPY AFTER SURGERY FOR BREAST CANCER WITH POSITIVE AXILLARY NODES

Kay, R. G., (Auckland 797-440, X-200) Auckland Hospital, Department of Surgery, Park Road, Auckland 3, New Zealand
PROTOCOL NUMBER(S) NZL-NBCG-1
CLOSING DATE: 11/80
PATIENT ACCRUAL: 01210280

GASTROINTESTINAL TUMORS

17.0026 ADJUVANT STUDY WITH 5-FLUOROURACIL PLUS METHYL CCNU FOLLOWING CURATIVE GASTRIC RESECTION FOR ADENOCARCINOMA OF THE STOMACH

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-3275
CLOSING DATE: 07/80

17.0027 ADJUVANT CHEMOTHERAPY WITH 5-FLUOROURACIL WITH OR WITHOUT METHYL CCNU FOLLOWING CURATIVE RESECTION FOR GASTRIC ADENOCARCINOMA

Lavin, P., (301-585-4844) Gastrointestinal Tumor Study Group, 850 Sligo Ave., Suite 601, Silver Spring, Maryland, 20910, United States of America
PROTOCOL NUMBER(S) GTSG-8174; MAYO-701891
CLOSING DATE: 09/80
PATIENT ACCRUAL: 01430279

17.0028 SURGICAL ADJUVANT COMBINATION CHEMOTHERAPY WITH 5-FU/MECCNU FOR CARCINOMA OF THE STOMACH

Higgins, G. A., (202-389-7266) Veterans Administration Surgical Oncology Group, 50 Irving St. N.W., Washington, District of Columbia, 20422, United States of America
PROTOCOL NUMBER(S) VASOG-30
CLOSING DATE: 05/80

17.0029 PHASE III CHEMOTHERAPY WITH MITOMYCIN-C/5-FU WITH OR WITHOUT STREPTOZOTOCIN FOR PANCREATIC ADENOCARCINOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7738
CLOSING DATE: 04/80
PATIENT ACCRUAL: 00580179

17.0030 PREOPERATIVE RADIOTHERAPY FOR RECTAL ADENOCARCINOMA

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-7785
CLOSING DATE: 04/80
PATIENT ACCRUAL: 00031078

17.0031 PHASE III 5-FU VS 5-FU/HU VS 5-FU/HU/MECCNU/DTIC VS MECCNU/DTIC VS MECCNU/ICRF VS MITO/DTIC FOR ADVANCED COLON AND RECTAL ADENOCARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1278
CLOSING DATE: 11/80

17.0032 ADJUVANT RADIATION THERAPY AFTER CURATIVE RESECTION OF RECTAL CANCER, DUKES B2 AND C

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-78GI344
CLOSING DATE: 02/80

17.0033 PHASE II CHEMOTHERAPY WITH 5-FLUOROURACIL VS 6-THIOGUANINE FOR INCURABLE OR RESISTANT ADENOCARCINOMA OF THE COLON

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-79GI268
CLOSING DATE: 07/80

17.0034 PHASE III CHEMOTHERAPY WITH 5-FU/MECCNU WITH OR WITHOUT ORAL BCG IMMUNOTHERAPY FOR LOCALLY ADVANCED ADENOCARCINOMA OF THE LARGE BOWEL

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7510
CLOSING DATE: 08/80
PATIENT ACCRUAL: 03931277

17.0035 ADJUVANT CHEMOTHERAPY WITH 5-FU BY PORTAL VEIN INFUSION FOR COLON ADENOCARCINOMA

Moertel, C. G., (507-282-2511, x3261) Gastrointestinal Tumor Study Group, 850 Sligo Ave., Suite 601, Silver Spring, Maryland, 20910, United States of America
PROTOCOL NUMBER(S) GTSG-6178
CLOSING DATE: 06/80

17.0036 ADJUVANT RADIOTHERAPY AND CHEMOTHERAPY WITH 5-FU/MECCNU FOLLOWING CURATIVE RESECTION FOR RECTAL ADENOCARCINOMA

Lavin, P., (301-585-4844) Gastrointestinal Tumor Study Group, 850 Sligo Ave., Suite 601, Silver Spring, Maryland, 20910, United States of America
PROTOCOL NUMBER(S) GTSG-7175; MAYO-754701; ITA-MIL-7505
CLOSING DATE: 09/80
PATIENT ACCRUAL: 01971278

17.0037 ADJUVANT IMMUNOTHERAPY WITH MER-BCG DURING RADIOTHERAPY FOR PRIMARY ADENOCARCINOMA OF THE RECTUM

Moertel, C. G., (507-282-2511, Ext. 3261) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-701872
CLOSING DATE: 01/80
PATIENT ACCRUAL: 00380379

17.0038 PHASE II CHEMOTHERAPY WITH INDICINE-N-OXIDE FOR ADVANCED COLORECTAL CANCER

Nichols, W. C., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-794601
CLOSING DATE: 03/80
TERMINATION DATE: 04/80

17.0039 PHASE II CHEMOTHERAPY WITH 6-THIOGUANINE FOR ADVANCED COLORECTAL ADENOCARCINOMA

Moertel, C., (507-282-2511 Ext. 3261) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-794605
CLOSING DATE: 03/80

17.0040 FUDR/MITO HEPATIC ARTERY INFUSION WITH OR WITHOUT C. PARVUM IMMUNOTHERAPY FOR LIVER METASTASES OF COLORECTAL CANCER

Patt, Y. Z., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-276; MDA-DT-7803
CLOSING DATE: 09/80

17.0041 PALA PLUS 5-FU INTRAVENOUS CHEMOTHERAPY GIVEN FOR 5 DAYS VS ONCE A WEEK FOR METASTATIC COLORECTAL CANCER

Valdivieso, M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-343; MDA-DT-7930
CLOSING DATE: 09/80

17.0042 CHEMOTHERAPY WITH 5-FU/MECCNU AND/OR IMMUNOTHERAPY WITH MER ADJUVANT TO SURGERY FOR COLORECTAL ADENOCARCINOMA

Krown, S., (212-794-7426) Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York, 10021, United States of America
PROTOCOL NUMBER(S) MSKCC-7368
CLOSING DATE: 01/80

17.0043 IMMUNOTHERAPY WITH MER-BCG ADJUVANT TO CHEMOTHERAPY WTH 5-FU/MECCNU FOR RESIDUAL COLORECTAL CARCINOMA

Higgins, G. A., (202-389-7266) Veterans Administration Surgical Oncology Group, 50 Irving St. N.W., Washington, District of Columbia, 20422, United States of America
PROTOCOL NUMBER(S) VASOG-27B
CLOSING DATE: 05/80

17.0044 ADJUVANT CHEMOTHERAPY WITH 5-FU VS 5-FU/HU FOR MALE PATIENTS FOLLOWING SURGERY FOR COLON OR RECTAL CANCER

Higgins, G. A., Veterans Administration Surgical Oncology Group, 50 Irving St. N.W., Washington, District of Columbia, 20422, United States of America
PROTOCOL NUMBER(S) VASOG-33
CLOSING DATE: 05/80

17.0045 POSTSURGICAL CHEMOTHERAPY WITH 5-FU VS VBL/THIOTEPA/STREPTONIGRIN/5-FU FOR COLORECTAL CARCINOMA, MODIFIED DUKES A, B, C1 OR C2

Jacquillat, C., (Paris 200.08.46) Hopital St. Louis, Chemotherapy Unit, 2 Pl. du Docteur Fournier, 75475 Paris 10, France
PROTOCOL NUMBER(S) FRE-UNCHIM-01CG76
CLOSING DATE: 07/80

17.0046 SINGLE VS MULTIPLE FRACTION RADIOTHERAPY FOLLOWED BY SURGERY FOR ADENOCARCINOMA OF THE RECTUM

Smith, A. N., ((031) 332.2525) Western General Hospital, Dept. of Clinical Surgery, Crewe Rd., Edinburgh 4, Scotland, United Kingdom
PROTOCOL NUMBER(S) UICC-76126; UKM-MRC-74-1033
CLOSING DATE: 09/80

17.0047 INTERMITTENT ADJUVANT IMMUNOTHERAPY WITH C. PARVUM FOLLOWING SURGERY FOR COLORECTAL CANCER

Gill, P. G., (Oxford 64841 Ext. 237) Radcliffe Infirmary, Dept. of Surgery, Woodstock Rd., Oxford OX2 6HE, England, United Kingdom
PROTOCOL NUMBER(S) UKM-OXF-8082; UKM-OXF-2
CLOSING DATE: 01/80

17.0048 RADIOTHERAPY AND 5-FLUOROURACIL CHEMOTHERAPY FOR LOCALLY UNRESECTABLE STOMACH, PANCREATIC, RECTAL AND BILIARY TRACT CANCER

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1274
CLOSING DATE: 07/80
PATIENT ACCRUAL: 01440778

17.0049 PHASE II CHEMOTHERAPY WITH CYCLIC DAILY ANGUIDINE FOR GASTROINTESTINAL TRACT ADENOCARCINOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-77GI0202; SEG-77GI221
CLOSING DATE: 07/80
PATIENT ACCRUAL: 00281078

17.0050 PHASE I-II CHEMOTHERAPY WITH ICRF-159/ADRIAMYCIN FOR ADVANCED METASTATIC ADENOCARCINOMA OF THE GASTROINTESTINAL TRACT

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-78GI0102; SEG-78GI238

CLOSING DATE: 01/80

17.0051 PHASE II CHEMOTHERAPY WITH M-AMSA FOR FAR ADVANCED GASTROINTESTINAL CANCER

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-79GI260
CLOSING DATE: 07/80

17.0052 PILOT AND PHASE II COMBINED CHEMOTHERAPY WITH FAP (ADR/CACP/5-FU) FOR ADVANCED GASTRIC AND PANCREATIC CARCINOMA

Moertel, C. G., (507-282-2511) Mayo Clinic, 200 1st Street, S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-790308/794801
CLOSING DATE: 07/80

17.0053 COMBINATION CHEMOTHERAPY WITH 5-FLUOROURACIL, VINDESINE, AND METHYL CCNU FOR METASTATIC GASTROINTESTINAL MALIGNANCIES

Valdivieso, M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-296; MDA-DT-7852
CLOSING DATE: 09/80
PATIENT ACCRUAL: 00400979

GENITOURINARY TUMORS

17.0054 PHASE I/II RADIOSENSITIZATION WITH MISONIDAZOLE PLUS RADIOTHERAPY FOR BLADDER CANCER

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7821
CLOSING DATE: 02/80
PATIENT ACCRUAL: 00020179

17.0055 VBL/CCNU, TZT, OR ACT-D, PALA, AMSA OR INDICINE CHEMOTHERAPY AND MASTER PHASE II PROTOCOL FOR ADVANCED RENAL CELL CANCER

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-3877
CLOSING DATE: 03/80
PATIENT ACCRUAL: 01270778

17.0056 INDUCTION AND MAINTENANCE CHEMOTHERAPY WITH YOSHI 864 PLUS HORMONE THERAPY WITH MPA FOR ADENOCARCINOMA OF THE KIDNEY IN ADULTS

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7805
CLOSING DATE: 03/80

17.0057 PHASE II PILOT CHEMOTHERAPY WITH TAMOXIFEN FOR ADVANCED CARCINOMA OF THE PROSTATE

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-PB-878
CLOSING DATE: 10/80

17.0058 CHEMOTHERAPY WITH CTX PLUS HORMONE THERAPY WITH ESTRACYT OR DES VS DES ALONE OR ORCHIECTOMY ALONE FOR STAGE D PROSTATIC CARCINOMA

Murphy, G. P., (716-845-5770) National Prostatic Cancer Project, 666 Elm St., c/o Roswell Park Mem. Inst., Buffalo, New York, 14263, United States of America
PROTOCOL NUMBER(S) NPCP-500
CLOSING DATE: 08/80

17.0059 HORMONE THERAPY WITH TAMOXIFEN FOR PROSTATIC CARCINOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-78GU232
CLOSING DATE: 02/80

17.0060 HORMONE THERAPY WITH DIETHYLSTILBESTROL PLUS IMMUNOTHERAPY WITH LEVAMISOLE IN STAGE D PROSTATE CANCER

Guinan, P., (312-633-6277) Cook County Hospital, Division of Urology, 1825 W. Harrison Street, Chicago, Illinois, 60612, United States of America
PROTOCOL NUMBER(S) IL-PR-2
CLOSING DATE: 06/80
PATIENT ACCRUAL: 00100280

17.0061 VAB III (CTX/ACT-D/VBL/BLEO) WITH HIGH VS LOW DOSE CACP FOLLOWED BY VAP OR AVP/CAP/VAP MAINTENANCE FOR TESTICULAR TUMORS

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1877
CLOSING DATE: 05/80

17.0062 CHEMOTHERAPY WITH CTX, VBL, ACT-D, BLEO, CACP, ADR FOR UNRESECTABLE STAGE II AND STAGE III NONSEMINOMATOUS GERM-CELL TUMORS

Golbey, R. B., (212-794-7093) Memorial Sloan Kettering Cancer Center, 1275 York Ave., New York, New York, 10021, United States of America
PROTOCOL NUMBER(S) MSKCC-7712
CLOSING DATE: 02/80

GYNECOLOGIC TUMORS

17.0063 PILOT IMMUNOTHERAPY WITH INTRAPERITONEAL BCG PLUS MELPHALAN/ISONIAZID CHEMOTHERAPY FOR STAGE IC, II OR III OVARIAN ADENOCARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America

PROTOCOL NUMBER(S) EST-PE-878

CLOSING DATE: 07/80

17.0064 PHASE III CHEMOTHERAPY WITH L-PAM FOLLOWED BY HAD (HMM/ADR/CACP) VS CHAD (CTX/ADR/HMM/CACP) FOR ADVANCED ADENOCARCINOMA OF THE OVARY

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America

PROTOCOL NUMBER(S) EST-2878

CLOSING DATE: 11/80

17.0065 PHASE II COMBINATION CHEMOTHERAPY WITH ACT-D/MTX/CLB FOR OVARIAN GERM CELL TUMORS CONTAINING CHORIOCARCINOMA

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) GOG-12

CLOSING DATE: 01/80

PATIENT ACCRUAL: 00070179

17.0066 PHASE II CHEMOTHERAPY WITH ACT-D/VCR PLUS RADIOTHERAPY FOLLOWED BY CTX/ACT-D FOR MIXED MESODERMAL OVARIAN TUMORS

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) GOG-13

CLOSING DATE: 06/80

PATIENT ACCRUAL: 00230179

17.0067 CHEMOTHERAPY WITH ADR PLUS VP-16 FOR STAGE III/IV ADENOCARCINOMA OF THE OVARY

Van Echo, D. A., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America

PROTOCOL NUMBER(S) BCRP-7827

CLOSING DATE: 03/80

17.0068 RELATION OF PROGESTIN RECEPTOR CONCENTRATION TO EFFICACY OF PROGESTIN THERAPY FOR ENDOMETRIAL ADENOCARCINOMA - PILOT STUDY

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) GOG-P12

CLOSING DATE: 01/80

PATIENT ACCRUAL: 00760778

17.0069 PHASE II HORMONE THERAPY WITH TAMOXIFEN FOR ADVANCED OR RECURRENT ENDOMETRIAL ADENOCARCINOMA

Lewis, G. C., (215-854-0770) Gynecologic Oncology Group, 1234 Market Street, Suite 430, Philadelphia, Pennsylvania, 19107, United States of America

PROTOCOL NUMBER(S) GOG-7892

CLOSING DATE: 04/80

TERMINATION DATE: 04/80

PATIENT ACCRUAL: 00010179

17.0070 CHEMOTHERAPY WITH 5-FU AND MEDROXYPROGESTERONE ACETATE AND WITH MELPHALAN FOR ADVANCED ENDOMETRIAL CARCINOMA

Pater, J. L., (613-544-9580) National Cancer Inst. of Canada, Clinical Trials Group, 12 O'Kill Street, Kingston, Ontario, K7L 5E2, Canada

PROTOCOL NUMBER(S) CAN-NCIC-TO-1; CAN-NCIC-EN1

CLOSING DATE: 00/80

TERMINATION DATE: 00/80

PATIENT ACCRUAL: 00410978

17.0071 PHASE II CHEMOTHERAPY WITH ADR/CTX WITH AND WITHOUT BCG IMMUNOTHERAPY FOR OVARIAN AND ENDOMETRIAL CARCINOMA, STAGES III AND IV

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7524

CLOSING DATE: 10/80

PATIENT ACCRUAL: 02020279

MYELOMA AND OTHER HEMATOLOGIC TUMORS

17.0072 PILOT PHASE II STUDY OF CHLOROZOTOCIN FOR MULTIPLE MYELOMA

Holland, J. F., (212-650-6364) Cancer and Leukemia Coop. Grp. B, 2 Overhill Road, Suite 208, Scarsdale, New York, 10583, United States of America

PROTOCOL NUMBER(S) CLB-7801

CLOSING DATE: 04/80

17.0073 PHASE I-II IMMUNOTHERAPY WITH POLY ICLC FOR MULTIPLE MYELOMA

Alexanian, R., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-388; MDA-M-8002

CLOSING DATE: 00/80

17.0074 PHASE II SEQUENTIAL HEMI-BODY RADIOTHERAPY FOR RECURRENT HISTIOCYTOSIS X IN CHILDREN

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America

PROTOCOL NUMBER(S) CCG-981

CLOSING DATE: 02/80

PROTOCOLS CLOSED IN 1980—Complete summaries available in CLINPROT data base

17.0075 CHEMOTHERAPY WITH CIMETIDINE FOR PRURITUS DUE TO POLYCYTHEMIA VERA

Wasserman, L., (212-876-2734) Polycythemia Vera Study Group, Dept. of Hematology, 19 E. 98th St., c/o Mount Sinai Hospital, New York, New York, 10029, United States of America

PROTOCOL NUMBER(S) PVSG-14

CLOSING DATE: 00/80

PATIENT ACCRUAL: 00120579

LEUKEMIA

17.0076 PHASE III VCR/L-ASP/PRED & DNM INDUCTION, 6-MP/MTX/VCR/PRED MAINTENANCE & MER-BCG FOR ACUTE LYMPHOCYTIC LEUKEMIA

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America

PROTOCOL NUMBER(S) CLB-7612

CLOSING DATE: 09/80

PATIENT ACCRUAL: 01041078

17.0077 PILOT INTENSIVE MTX/CF CONSOLIDATION THERAPY WITH PROTOCOL CLB-7611 INDUCTION AND MAINTENANCE FOR HIGH-RISK ALL IN CHILDREN

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America

PROTOCOL NUMBER(S) CLB-7901

CLOSING DATE: 06/80

17.0078 PHASE I STUDY OF 2 PRIME-DEOXYCOFORMYCIN IN ACUTE LYMPHOBLASTIC LEUKEMIA

Poplack, D. G., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America

PROTOCOL NUMBER(S) NCI-79-C-103; NCI-POB-7903

CLOSING DATE: 10/80

17.0079 VCR/DNM/PRED INDUCTION WITH OR WITHOUT L-ASP, ARA-C, CNS RADIOTHERAPY PLUS MTX, AND MAINTENANCE WITH 6-MP/MTX FOR CHILDREN WITH ALL

Aur, R. J., (901-525-8381) St. Jude Childrens Research Hospital, 332 N. Lauderdale St., P.O. Box 318, Memphis, Tennessee, 38101, United States of America

PROTOCOL NUMBER(S) SJCRH-ALL-TT-9

CLOSING DATE: 01/80

17.0080 COMBINATION CHEMOTHERAPY WITH VCR/PRDL WITH OR WITHOUT REINFORCEMENT AND 6-MP/MTX FOR NON-T CELL ACUTE LYMPHOCYTIC LEUKEMIA IN CHILDREN

Shetty, P. A., Tata Memorial Hospital, Department of Chemotherapy, Bombay 400 012, India

PROTOCOL NUMBER(S) INA-TAT-TMC1

CLOSING DATE: 12/80

17.0081 COMBINATION CHEMOTHERAPY WITH ROAP (RBD/ARA-C/VCR/PRED), POMP (6-MP/MTX/VCR/PRED) AND OAP (ARA-C/VCR/PRED) PLUS TG WITH OR WITHOUT MER FOR AML

Keating, M. J., (713-792-2121) University of Texas, M.D. Anderson Hospital and Tumor Inst., Houston, Texas, 77030, United States of America

PROTOCOL NUMBER(S) MDAR-336; MDA-DT-7926

CLOSING DATE: 09/80

17.0082 ALLOGENEIC TUMOR CELLS DURING INTENSIVE MAINTENANCE CHEMOTHERAPY AFTER INDUCTION WITH ARA-C/ADR FOR ACUTE MYELOCYTIC LEUKEMIA

Preisler, H. D., (716-845-3352) Roswell Park Memorial Institute, Dept. of Medicine A, 666 Elm Street, Buffalo, New York, 14263, United States of America

PROTOCOL NUMBER(S) RPMI-DMA-970701

CLOSING DATE: 00/80

17.0083 CHEMOTHERAPY WITH VCR, DNM, ARA-C, AZUR, MTX, L-ASP, ADR, CTX AND 6-MP WITH OR WITHOUT SPLENECTOMY FOR ACUTE NONLYMPHOCYTIC LEUKEMIA

Simone, J., (901-525-8381) St. Jude Childrens Research Hospital, 332 N. Lauderdale St., P.O. Box 318, Memphis, Tennessee, 38101, United States of America

PROTOCOL NUMBER(S) SJCRH-AML-76

CLOSING DATE: 03/80

17.0084 MAINTENANCE CHEMOTHERAPY WITH DNM, ARA-C, 6-MP, PRDL, VCR, CTX WITH AND WITHOUT NOCARDIA RUBRA CWS AND ALLOGENEIC LEUKEMIA CELLS IN ANLL

Yamada, K., Nagoya University of Medicine, First Dept. of Internal Medicine, 65 Tsurumai-cho, Showaku, Nagoya 466, Japan

PROTOCOL NUMBER(S) JAP-ANLL-N-CWS-1

CLOSING DATE: 12/80

PATIENT ACCRUAL: 00300280

17.0085 PHASE III CHEMOTHERAPY WITH CLB/PRED AND CTX/ARA-C/PRED VS TOTAL BODY RADIOTHERAPY FOR CHRONIC LYMPHOCYTIC LEUKEMIA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America

PROTOCOL NUMBER(S) EST-3476

CLOSING DATE: 06/80

PATIENT ACCRUAL: 00500379

17.0086 PHASE II CHEMOTHERAPY WITH NEOCARZINOSTATIN FOR ACUTE LYMPHOCYTIC OR ACUTE NONLYMPHOCYTIC LEUKEMIA IN CHILDREN

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America

PROTOCOL NUMBER(S) SWOG-7831; MDAR-319

CLOSING DATE: 04/80

LUNG TUMORS

17.0087 PILOT STUDY CHEMOTHERAPY WITH CCM INDUCTION AND RADIOTHERAPY CONSOLIDATION OF SMALL CELL UNDIFFERENTIATED LUNG CARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-PB-579
CLOSING DATE: 12/80

17.0088 PHASE I-II CHEMOTHERAPY WITH VP-16/CCNU/PROCARBAZINE FOR DISSEMINATED SMALL CELL CARCINOMA OF THE LUNG

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-LUN-P31
CLOSING DATE: 03/80

17.0089 PHASE II CHEMOTHERAPY WITH ACRIDINYL ANISIDIDE (M-AMSA) FOR ADVANCED SMALL CELL CARCINOMA OF THE LUNG

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-80LUN271
CLOSING DATE: 07/80

17.0090 MEGADOSE CHEMOTHERAPY WITH VCR/CTX/VP-16/BCNU WITH AUTOLOGOUS BONE MARROW RESCUE FOR OAT CELL CARCINOMA OF THE LUNG

Dicke, K. A., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-235; MDA-DT-7738
CLOSING DATE: 09/80

17.0091 CHEMOTHERAPY IN PEPA WITH ECHO (VP-16/CTX/ADR/VCR) PLUS PRIME (PCB/IPP/MTX) PLUS RADIOTHERAPY FOR SMALL CELL LUNG CANCER

Valdivieso, M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-267; MDA-DT-7809
CLOSING DATE: 09/80

17.0092 VP-16/CTX/ADR/VCR AND PCB/IPP/MTX WITH OR WITHOUT INTRAVENOUS HYPERALIMENTATION FOR SMALL CELL BRONCHOGENIC CARCINOMA

Valdivieso, M., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-290; MDA-DT-7835
CLOSING DATE: 09/80
PATIENT ACCRUAL: 00620979

17.0093 CTX/ADR/VCR INDUCTION WITH ADDED CCNU/MTX/PCB OR CTX/VCR PLUS RADIOTHERAPY CONSOLIDATION FOR SMALL CELL LUNG CANCER

Wittes, R. E., (212-794-7646) Memorial Sloan Kettering Cancer Center, 1275 York Ave., New York, New York, 10021, United States of America
PROTOCOL NUMBER(S) MSKCC-7891
CLOSING DATE: 02/80

17.0094 CHEMOTHERAPY WITH MTX VS MTX PLUS IMMUNOTHERAPY IN LIMITED STAGE SMALL CELL LUNG CANCER WITH PRIOR COMBINATION CHEMO AND RADIATION THERAPY

Greco, F. A., (615-322-4967) Vanderbilt University, Dept. of Medicine, Division of Oncology, Nashville, Tennessee, 37232, United States of America
PROTOCOL NUMBER(S) TN-LUN-L38
CLOSING DATE: 03/80
PATIENT ACCRUAL: 00750380

17.0095 RADIOTHERAPY PLUS HAM (HMM/ADR/MTX) CHEMOTHERAPY FOR NONRESECTABLE NON-OAT-CELL LUNG CANCER

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-PD-578
CLOSING DATE: 07/80

17.0096 PHASE II MASTER PROTOCOL AND TRIALS WITH AMSA AND NEOCARZINOSTATIN FOR NON-SMALL CELL LUNG CARCINOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1579
CLOSING DATE: 07/80

17.0097 PHASE I/II STUDY OF HYPOXIC CELL SENSITIZER MISONIDAZOLE PLUS RADIOTHERAPY FOR LOCALLY ADVANCED LUNG CARCINOMA

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7814
CLOSING DATE: 01/80
PATIENT ACCRUAL: 00040179

17.0098 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR REFRACTORY EPIDERMOID CARCINOMA OF THE LUNG

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7807
CLOSING DATE: 04/80
PATIENT ACCRUAL: 00090978

PROTOCOLS CLOSED IN 1980—Complete summaries available in CLINPROT data base

17.0099 PHASE II/PILOT COMBINATION CHEMOTHERAPY WITH MITO/DAVA/5-FU FOR ADENOCARCINOMA AND LARGE CELL CARCINOMA OF THE LUNG

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7971
CLOSING DATE: 10/80

17.0100 PHASE II EVALUATION OF ME-GAG IN THE TREATMENT OF INCURABLE, ADVANCED, METASTATIC NON-OAT CELL CARCINOMA OF THE LUNG

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-8003
CLOSING DATE: 10/80

17.0101 ADJUVANT IMMUNOTHERAPY WITH POSTOPERATIVE INTRAPLEURAL BCG FOR LUNG CARCINOMA

McGuire, W. P., (301-496-2522) Lung Cancer Study Group, 7910 Woodmont Ave., Room C804, c/o Natl. Canc. Inst., Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) LCSG-771
CLOSING DATE: 10/80
PATIENT ACCRUAL: 02470279

17.0102 PHASE II CHEMOTHERAPY WITH DAP-II (DAG/ADR/CACP) FOLLOWED BY CTX/VP-16 FOR ADVANCED SQUAMOUS CELL LUNG CANCER

Eagan, R. T., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-772203
CLOSING DATE: 02/80
PATIENT ACCRUAL: 00080279

17.0103 VP-16/CYCLOPHOSPHAMIDE/ADRIAMYCIN/CIS-PLATINUM FOR ADVANCED LARGE CELL LUNG CANCER

Eagan, R. T., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-782301
CLOSING DATE: 04/80
PATIENT ACCRUAL: 00060279

17.0104 PHASE II CHEMOTHERAPY WITH AMSA FOR ADVANCED LUNG CANCER

Eagan, R. T., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-782502
CLOSING DATE: 03/80

17.0105 PHASE II CHEMOTHERAPY WITH INTERMITTENT DIBROMODULCITOL FOR ADVANCED NON-SMALL CELL LUNG CANCER

Moertel, C., (507-282-2511 Ext. 3261) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-792402
CLOSING DATE: 04/80

17.0106 PHASE II CHEMOTHERAPY WITH AMSA FOR METASTATIC LUNG CANCER REFRACTORY TO PRIMARY THERAPY

Murphy, W. K., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-286; MDA-DT-7839
CLOSING DATE: 09/80
PATIENT ACCRUAL: 00470679

17.0107 VAP (DAVA/ADR/CACP) CHEMOTHERAPY WITH/WITHOUT THYMOSIN FOR METASTATIC DISSEMINATED NON-OAT CELL LUNG CARCINOMA

Bedikian, A. Y., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-318; MDA-DT-7902
CLOSING DATE: 09/80

17.0108 COMBINATION CHEMOTHERAPY WITH HIGH VS LOW DOSE CIS-PLATINUM/VINDESINE FOR NON SMALL CELL LUNG CANCER

Gralla, R. J., (212-794-7093) Memorial Sloan Kettering Cancer Center, 1275 York Ave., New York, New York, 10021, United States of America
PROTOCOL NUMBER(S) MSKCC-786
CLOSING DATE: 02/80

17.0109 COMBINATION CHEMOTHERAPY WITH CACP/ADR/CTX/DAVA VS CACP/CTX/DAVA FOR UNRESECTABLE OR METASTATIC NON-SMALL CELL LUNG CANCER

Kelsen, D. P., (212-794-7617) Memorial Sloan Kettering Cancer Center, 1275 York Ave., New York, New York, 10021, United States of America
PROTOCOL NUMBER(S) MSKCC-7942
CLOSING DATE: 08/80

17.0110 PHASE II CHEMOTHERAPY WITH ADR/MITO IN ADVANCED NON-SMALL CELL CARCINOMA OF THE LUNG

West, W. H., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-79-C-37; NCI-VA-MOB-784
CLOSING DATE: 05/80

17.0111 INTRAPLEURAL VS INTRADERMAL BCG FOR NON-SMALL CELL CARCINOMA OF THE LUNG WITHOUT LYMPHNODE METASTASES

Higgins, G. A., (202-389-7266) Veterans Administration Surgical Oncology Group, 50 Irving St. N.W., Washington, District of Columbia, 20422, United States of America
PROTOCOL NUMBER(S) VASOG-34A
CLOSING DATE: 05/80

17.0112 POSTSURGICAL RADIOTHERAPY FOR RESECTED NON-SMALL CELL CARCINOMA OF THE LUNG WITH LYMPHNODE METASTASES

Higgins, G. A., (202-389-7266) Veterans Administration Surgical Oncology Group, 50 Irving St. N.W., Washington, District of Columbia, 20422, United States of America
PROTOCOL NUMBER(S) VASOG-34B
CLOSING DATE: 05/80

17.0113 PHASE III IMMUNOTHERAPY WITH NOCARDIA RUBRA CELL WALL SKELETON FOR LUNG CANCER

Yamamura, Y., Osaka University Medical School, Third Dept. of Internal Medicine, Fukushima-ku, Osaka, 553, Japan
PROTOCOL NUMBER(S) JAP-LC-N-CWS
CLOSING DATE: 12/80
PATIENT ACCRUAL: 02940280

17.0114 ADJUVANT IMMUNOTHERAPY WITH NOCARDIA RUBRA CELL WALL SKELETON (N-CWS) AFTER INDUCTION CHEMOTHERAPY WITH MITOMYCIN-C FOR LUNG CANCER

Yamamura, Y., Osaka University Medical School, Third Dept. of Internal Medicine, Fukushima-ku, Osaka, 553, Japan
PROTOCOL NUMBER(S) JAP-PL-N-CWS
CLOSING DATE: 12/80
PATIENT ACCRUAL: 00520280

17.0115 SPECIFIC IMMUNOTHERAPY WITH IRRADIATED AUTOLOGOUS TUMOR CELLS AND CORYNEBACTERIUM PARVUM FOR RESECTABLE LUNG CANCER

Gill, P. G., (Oxford 64841 Ext. 237) Radcliffe Infirmary, Dept. of Surgery, Woodstock Rd., Oxford OX2 6HE, England, United Kingdom
PROTOCOL NUMBER(S) UKM-OXF-8081; UKM-OXF-1
CLOSING DATE: 01/80

LYMPHOMA

17.0116 RADIOTHERAPY PLUS CHEMOTHERAPY WITH NM/VCR/PCB/PRED/BLEO VS CHEMOTHERAPY FOR STAGE III A & B HODGKIN'S DISEASE - A PHASE III STUDY

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7518; MDAR-24
CLOSING DATE: 04/80
PATIENT ACCRUAL: 01050379

17.0117 MOPP CHEMOTHERAPY WITH OR WITHOUT ABVD WITH LOW OR HIGH DOSE RADIOTHERAPY FOR STAGE III AND IV HODGKIN'S DISEASE

Pater, J. L., (613-544-9580) National Cancer Inst. of Canada, Clinical Trials Group, 12 O'Kill Street, Kingston, Ontario, K7L 5E2, Canada
PROTOCOL NUMBER(S) CAN-NCIC-HD3
CLOSING DATE: 05/80

17.0118 MULTIMODALITY THERAPY FOR THE INDUCTION, CNS PROPHYLAXIS AND MAINTENANCE OF NON-HODGKIN'S LYMPHOMA

Murphy, S. B., (901-525-8381) St. Jude Childrens Research Hospital, 332 N. Lauderdale St., P.O. Box 318, Memphis, Tennessee, 38101, United States of America
PROTOCOL NUMBER(S) SJCRH-NHL-75
CLOSING DATE: 05/80

17.0119 ADR, ARA-C, BLEO, CLB, CTX, PRED, TG, VCR COMBINATION CHEMOTHERAPY WITH AND WITHOUT RADIOTHERAPY & HORMONE THERAPY IN NON-HODGKIN'S LYMPHOMA

deAcquatella, G., Hospital Universitario de Caracas, Apartado 10588, Sabana Grande, Caracas, Venezuela
PROTOCOL NUMBER(S) VEN-NHL-1
CLOSING DATE: 07/80

17.0120 PHASE II MASTER PROTOCOL AND CHEMOTHERAPY WITH VM-26/PRED PLUS CIS-PLATINUM OR HEXAMETHYLMELAMINE FOR LYMPHOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1478
CLOSING DATE: 04/80

17.0121 PHASE II CHEMOTHERAPY WITH MAYTANSINE FOR ADVANCED HODGKIN'S AND NON-HODGKIN'S LYMPHOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7821
CLOSING DATE: 04/80

17.0122 MULTIPLE MODALITY TREATMENT FOR LYMPHOSARCOMA AND RETICULUM CELL SARCOMA

Benjamin, R. S., Baltimore Cancer Research Program, Division of Cancer Treatment, National Cancer Institute, 22 S. Greene Street, Baltimore, Maryland, 21201, United States of America
PROTOCOL NUMBER(S) BCRP-7101A
CLOSING DATE: 11/75

MELANOMA AND OTHER SKIN CANCERS

17.0123 PHASE II PILOT STUDY WITH AMSA FOR METASTATIC MALIGNANT MELANOMA

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-PC-678
CLOSING DATE: 07/80

17.0124 PHASE II CHEMOTHERAPY WITH BLEO, CACP, OR BCNU WITH/WITHOUT HYPERTHERMIA FOR SUPERFICIAL LESIONS

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7919
CLOSING DATE: 09/80

17.0125 PHASE III STUDY OF ADJUVANT IMMUNOTHERAPY WITH CORYNEBACTERIUM PARVUM VACCINE FOR STAGE II MELANOMA

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-360

CLOSING DATE: 07/80

17.0126 PHASE II EVALUATION OF TAMOXIFEN IN PATIENTS WITH RECURRENT MALIGNANT MELANOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Boulevard, Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7874
CLOSING DATE: 05/80

17.0127 PHASE II CHEMOTHERAPY WITH PALA AND/OR AMSA FOR ADVANCED MALIGNANT MELANOMA

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-787003
CLOSING DATE: 06/80

17.0128 PHASE II CHEMOTHERAPY WITH AMSA WITH OR WITHOUT DTIC FOR METASTATIC MALIGNANT MELANOMA

Legha, S. S., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-317; MDA-DT-7868
CLOSING DATE: 09/80

17.0129 DEEP INGUINAL LYMPH NODE DISSECTION FOR MALIGNANT MELANOMA WITH POSITIVE SUPERFICIAL INGUINAL NODES

Cohen, M. H., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-77-C-151
CLOSING DATE: 07/80
TERMINATION DATE: 07/80

17.0130 IMMUNOTHERAPY WITH DINITROCHLOROBENZENE FOR MULTIPLE SKIN TUMORS

Levis, W. R., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-77-C-154
CLOSING DATE: 09/80
TERMINATION DATE: 09/80

17.0131 TOPICAL IMMUNOTHERAPY OF CUTANEOUS MALIGNANCIES WITH CONTACT SENSITIZERS

Levis, W. R., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-78-C-79
CLOSING DATE: 09/80
TERMINATION DATE: 09/80

17.0132 ADJUVANT IMMUNOTHERAPY WITH BCG IN STAGE 1 MALIGNANT MELANOMA

Paterson, A. H., (403-432-8521) Cross Cancer Institute, Department of Medicine, 11560 University Avenue, Edmonton, Alberta, T6G 1Z2, Canada
PROTOCOL NUMBER(S) CAN-CCI-MEL-1
CLOSING DATE: 00/80

PATIENT ACCRUAL: 01420080

17.0133 DTIC/VBL/THIOTEPA/MTX/STREPTONIGRIN/PROCARBAZINE WITH OR WITHOUT BCG/C. PARVUM FOR MELANOMA

Jacquillat, C., (Paris 200.08.46) Hopital St. Louis, Chemotherapy Unit, 2 Pl. du Docteur Fournier, 75475 Paris 10, France
PROTOCOL NUMBER(S) FRE-UNCHIM-4NK76
CLOSING DATE: 12/80

17.0134 ADJUVANT CHEMOTHERAPY AND IMMUNOTHERAPY FOR RESECTED CUTANEOUS MELANOMA WITH OR WITHOUT REGIONAL LYMPH-NODE METASTASES

Veronesi, U., (Milan (02) 2390, Ext. 206) Istituto Nazionale per lo Studio e la Cura dei Tumori, 1 Via Venezian, 20133 Milan, Italy
PROTOCOL NUMBER(S) UICC-73052; ITA-IGM-6
CLOSING DATE: 00/80

17.0135 CHEMOTHERAPY WITH DTIC PLUS IMMUNOTHERAPY WITH BCG OR C. PARVUM FOR ADVANCED AND METASTATIC MELANOMA

Veronesi, U., (Milan (02) 2390, Ext. 206) Istituto Nazionale per lo Studio e la Cura dei Tumori, Eval Methods Diag Treat Melanoma, 1 Via Venezian, 20133 Milan, Italy
PROTOCOL NUMBER(S) UICC-76016; ITA-IGM-8
CLOSING DATE: 00/80

SARCOMA

17.0136 ADJUVANT CHEMOTHERAPY WITH ADR VS. ADR/MTX/CF VS. ADR/CTX FOLLOWING SURGERY FOR OSTEOGENIC SARCOMA

Holland, J. F., (212-650-6364) Cancer & Leukemia Coop. Grp. B, 2 Overhill Rd., Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-7583
CLOSING DATE: 04/80
PATIENT ACCRUAL: 00741078

17.0137 OPTIMAL FRACTIONATION SCHEDULE OF PALLIATIVE RADIOTHERAPY FOR RELIEF OF PAIN DUE TO OSSEOUS METASTASES

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7402; RTOG-1074; RTOG-8174
CLOSING DATE: 02/80
PATIENT ACCRUAL: 10000179

17.0138 PHASE II CHEMOTHERAPY WITH 5-AZACYTIDINE FOR REFRACTORY OSTEOGENIC SARCOMA AND EWING'S SARCOMA

Reaman, G. H., National Cancer Institute, Division of Cancer Treatment, Clinical Oncology Program, Bldg. 10, Room 6B15, Bethesda, Maryland, 20205, United States of America
PROTOCOL NUMBER(S) NCI-78-C-64; NCI-POB-7802
CLOSING DATE: 10/80

17.0139 CIS-PLATINUM FOR REFRACTORY UNRESECTABLE OSTEOSARCOMA

Pater, J. L., (613-544-9580) National Cancer Inst. of Canada, Clinical Trials Group, 12 O'Kill Street, Kingston, Ontario, K7L 5E2, Canada
PROTOCOL NUMBER(S) CAN-NCIC-7702; CAN-NCIC-OS2
CLOSING DATE: 05/80

17.0140 CONCURRENT VS SEQUENTIAL COMBINATION CHEMOTHERAPY WITH ADR/MTX/CF FOR OSTEOGENIC SARCOMA

Pater, J. L., (613-544-9580) National Cancer Inst. of Canada, Clinical Trials Group, 12 O'Kill Street, Kingston, Ontario, K7L 5E2, Canada
PROTOCOL NUMBER(S) CAN-UICC-76001; CAN-NCIC-TO-2; UICC-76001; CAN-NCIC-OS1
CLOSING DATE: 00/80
TERMINATION DATE: 00/80

17.0141 PHASE III ADJUVANT RADIOTHERAPY WITH AND WITHOUT CHEMOTHERAPY WITH DTIC/ADRIAMYCIN FOR SOFT TISSUE SARCOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7802; MDAR-278
CLOSING DATE: 02/80

17.0142 PHASE II CHEMOTHERAPY WITH LOW-DOSE METHOTREXATE FOR REFRACTORY SOFT TISSUE SARCOMA

Brugarolas, A., (Spain 985-230000 X471) European Org. for Research on Treatment of Cancer, Soft Tissue and Bone Sarcoma Coop. Grp., Hospital General de Asturias, Oviedo, Spain
PROTOCOL NUMBER(S) EORTC-62792
CLOSING DATE: 03/80

17.0143 PHASE III ADJUVANT STUDY OF IMMUNOTHERAPY WITH C. PARVUM AND CHEMOTHERAPY WITH CAM (CTX/ADR/MTX) IN SOFT TISSUE AND BONE SARCOMAS

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-77SAR0103; SEG-77SAR316
CLOSING DATE: 02/80
PATIENT ACCRUAL: 00211078

17.0144 PHASE II CHEMOTHERAPY WITH GALLIUM NITRATE FOR INCURABLE ADVANCED SOFT TISSUE AND BONE SARCOMAS

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7911
CLOSING DATE: 04/80

PEDIATRIC SOLID TUMORS

17.0145 PREOPERATIVE AND POSTOPERATIVE RADIOTHERAPY AND CHEMOTHERAPY WITH ACT-D/VCR FOR WILMS' TUMOR

Voute, P. A., (Amsterdam 020-22-02-80) S.I.O.P. Nephroblastoma Trial and Study Office, Emma Kinderziekenhuis, Spinozastraat 51, 1018 HJ Amsterdam, The Netherlands
PROTOCOL NUMBER(S) UICC-76068; SIOP-5
CLOSING DATE: 01/80

17.0146 PHASE III PILOT STUDY WITH CTX/VCR/DTIC FOLLOWED BY CTX/ADR ALTERNATING WITH VM-26 FOR STAGE III AND IV CHILDHOOD NEUROBLASTOMA

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-371P/373P
CLOSING DATE: 01/80

17.0147 PHASE II CHEMOTHERAPY WITH AZAPICYL FOR RHABDOMYOSARCOMA AND UNDIFFERENTIATED SARCOMA IN CHILDREN

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-075
CLOSING DATE: 02/80
PATIENT ACCRUAL: 00060279

17.0148 CHEMOTHERAPY WITH VAC (VCR/ACT-D/CTX) AND VADRC (VCR/ADR/CTX) PLUS RADIOTHERAPY AND/OR SURGERY FOR PRIMARY PELVIC RHABDOMYOSARCOMA

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7898; IRS-II; CCG-681, MDAR-321; CLB-7891
CLOSING DATE: 03/80
TERMINATION DATE: 03/80

17.0149 HIGH VS MODERATE DOSE CHEMOTHERAPY WITH VCR/ADR/CTX/ACT-D PLUS RADIOTHERAPY FOLLOWING SURGERY FOR PRIMARY EWING'S SARCOMA OF BONE

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7896; CCG-784; MDAR-322; CLB-7893
CLOSING DATE: 03/80
TERMINATION DATE: 03/80

17.0150 PHASE II CHEMOTHERAPY WITH CIS-PLATINUM FOR CHILDREN WITH VARIOUS ADVANCED SOLID TUMORS

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-071
CLOSING DATE: 02/80
PATIENT ACCRUAL: 01140279

17.0151 ADJUVANT PHASE III CHEMOTHERAPY WITH CTX/VCR FOR CHILDHOOD LOCALIZED UNILATERAL RETINOBLASTOMA

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-961; SWOG-7796
CLOSING DATE: 10/80
PATIENT ACCRUAL: 00480279

17.0152 PHASE III CHEMOTHERAPY WITH CTX/VCR OR CTX/VCR/ADR/MTX PLUS RADIOTHERAPY FOR EXTRAOCULAR RETINOBLASTOMA

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-962; SWOG-7994; MDAR-361
CLOSING DATE: 10/80
PATIENT ACCRUAL: 00090279

HEAD AND NECK TUMORS

17.0153 ADJUVANT CHEMOTHERAPY WITH MTX AND IMMUNOTHERAPY WITH C. PARVUM FOR STAGE III-IV SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1375
CLOSING DATE: 06/80
PATIENT ACCRUAL: 00560878

17.0154 PHASE III THERAPY WITH MTX WITH OR WITHOUT C. PARVUM OR BLEO/CACP FOR ADVANCED SQUAMOUS CELL CANCER OF THE HEAD AND NECK

Carbone, P., (608-263-6650) Eastern Cooperative Oncology Group, 905 University Ave., Suite 415, Madison, Wisconsin, 53715, United States of America
PROTOCOL NUMBER(S) EST-1377
CLOSING DATE: 11/80
PATIENT ACCRUAL: 00220878

17.0155 REGISTRY OF HEAD AND NECK TUMORS TREATED WITH RADIOTHERAPY ALONE OR IN COMBINATION WITH SURGERY AND/OR CHEMOTHERAPY

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7619
CLOSING DATE: 02/80
PATIENT ACCRUAL: 06820478

17.0156 PHASE II CHEMOTHERAPY WITH CTX/ADR/CACP FOLLOWED UPON FAILURE BY MAYTANSINE FOR ADVANCED HEAD AND NECK CANCER

Creagan, E. T., (507-282-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-777401
CLOSING DATE: 02/80
TERMINATION DATE: 04/80
PATIENT ACCRUAL: 00370279

17.0157 PHASE II CHEMOTHERAPY WITH PALA FOR ADVANCED HEAD AND NECK CANCER

Creagan, E. T., (507-262-2511) Mayo Clinic, 200 1st St. S.W., Rochester, Minnesota, 55901, United States of America
PROTOCOL NUMBER(S) MAYO-787402
CLOSING DATE: 07/80
TERMINATION DATE: 07/80

17.0158 MTX VS MTX ALTERNATING WITH VBL/BLEO CHEMOTHERAPY FOLLOWING CURATIVE RADIOTHERAPY FOR LOCALLY ADVANCED CARCINOMA OF THE OROPHARYNX

Bertrand, M., (Brussels (02) 538.65.33) Head & Neck Cooperative Group, 1 Rue Heger Bordet, c/o Inst. Jules Bordet, Brussels, 1000, Belgium
PROTOCOL NUMBER(S) UICC-76003; EORTC-OROPH-2
CLOSING DATE: 10/80

BRAIN AND OTHER CNS TUMORS

17.0159 PHASE III COMBINATION CHEMOTHERAPY WITH VCR/CCNU/PRED VS PCB & RADIOTHERAPY FOR BRAIN STEM TUMORS IN CHILDREN

Hammond, D., (213-226-2008) Childrens Cancer Study Group, 1721 Griffin Ave., c/o U. of S. Calif. Canc. Ctr., Los Angeles, California, 90031, United States of America
PROTOCOL NUMBER(S) CCG-944
CLOSING DATE: 10/80
PATIENT ACCRUAL: 00490279

17.0160 PHASE I-II MISONIDAZOLE RADIOSENSITIZATION PRIOR TO RADIOTHERAPY FOR RECURRENT BRAIN TUMORS IN CHILDREN

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7823; CCG-985
CLOSING DATE: 10/80

17.0161 COMBINATION CHEMOTHERAPY WITH CCNU/HU AND RADIOTHERAPY FOR ASTROCYTOMA GRADES III AND IV

Keen, C. W., (416-924-0671) Princess Margaret Hospital, Radiation Oncology, 500 Sherbourne St., Toronto, Ontario, M4X 1K9, Canada
PROTOCOL NUMBER(S) CAN-UICC-76103; UICC-76103
CLOSING DATE: 03/80

17.0162 PHASE II COMBINATION CHEMOTHERAPY WITH LOW-DOSE DDMP/CITROVORUM FACTOR FOR RECURRENT BRAIN GLIOMAS

Calliauw, L., European Org. for Research on Treatment of Cancer, Brain Tumors Cooperative Group, Afdeling Neurochirurgie, St. Jan's Hospital, 8000 Brugge, Belgium
PROTOCOL NUMBER(S) EORTC-26782
CLOSING DATE: 05/80

17.0163 VM-26 CHEMOTHERAPY FOR TUMORS OF THE CENTRAL NERVOUS SYSTEM

Garbino, C. E., Hospital de Clinicas, planta baja, Depto. y Catedra de Oncologia, Av. Italia s/n y Las Heras, Montevideo, Uruguay
PROTOCOL NUMBER(S) URU-CNS-64
CLOSING DATE: 12/80

UNSPECIFIED OR MULTIPLE NEOPLASMS

17.0164 PHASE II CHEMOTHERAPY WITH NEOCARZINOSTATIN FOR ACUTE LEUKEMIA AND FOR VARIOUS SOLID TUMORS

Holland, J. F., (212-650-6364) Cancer & Leukemia Cooperative Group B, 2 Overhill Road, Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-0704
CLOSING DATE: 02/80
PATIENT ACCRUAL: 00871178

17.0165 PILOT-PHASE II CHEMOTHERAPY WITH INOX FOR ADVANCED TESTICULAR CANCER, MELANOMA, OAT CELL CARCINOMA, AND SARCOMA

Holland, J. F., (212-650-6364) Cancer and Leukemia Coop. Grp. B, 2 Overhill Road, Suite 208, Scarsdale, New York, 10583, United States of America
PROTOCOL NUMBER(S) CLB-7701
CLOSING DATE: 04/80

17.0166 PHASE I-II STUDY OF RADIOTHERAPY AND/OR HYPERTHERMIA FOR SUPERFICIAL HUMAN TUMORS

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7710
CLOSING DATE: 02/80
PATIENT ACCRUAL: 00220179

17.0167 PHASE I-II HYPERTHERMIA (43.5 DEGREES CENTIGRADE) BEFORE AND AFTER RADIATION TREATMENT FOR HUMAN TUMORS

Brady, L., (215-574-3150) Radiation Therapy Oncology Group, 925 Chestnut St., 7th Floor, Philadelphia, Pennsylvania, 19107, United States of America
PROTOCOL NUMBER(S) RTOG-7816
CLOSING DATE: 02/80

17.0168 PHASE II HMM THERAPY FOR HODGKIN'S & NON-HODGKIN'S LYMPHOMA, CHRONIC LYMPHOCYTIC LEUKEMIA, AND CARCINOMA OF THE OVARY & CERVIX

Durant, J. R., (205-934-5077) Southeastern Cancer Study Group, Comprehensive Cancer Center, University of Alabama, Birmingham, Tumor Inst., Room 225, Birmingham, Alabama, 35294, United States of America
PROTOCOL NUMBER(S) SEG-267R
CLOSING DATE: 05/80
PATIENT ACCRUAL: 01780878

17.0169 PHASE II PILOT CHEMOTHERAPY WITH METHYL-GAG FOR SOLID TUMORS AND REFRACTORY HEMATOLOGIC MALIGNANCIES

Hoogstraten, B., (913-588-5996) Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas City, Kansas, 66103, United States of America
PROTOCOL NUMBER(S) SWOG-7860
CLOSING DATE: 05/80
PATIENT ACCRUAL: 01170279

17.0170 PHASE II CHEMOTHERAPY WITH NZS FOR CHRONIC AND ACUTE LEUKEMIAS, LYMPHOMA, AND LIVER, RENAL, AND BLADDER CARCINOMAS

McKelvey, M. E., (713-792-2121) University of Texas, M.D. Anderson Hospital & Tumor Inst., Houston, Texas, 77030, United States of America
PROTOCOL NUMBER(S) MDAR-228; MDA-DT-7534A
CLOSING DATE: 09/80
PATIENT ACCRUAL: 00560679

17.0171 IMMUNOTHERAPY WITH TRANSFER FACTOR FOR MEASURABLE CANCER

Pinsky, C. M., (212-794-7595) Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York, 10021, United States of America
PROTOCOL NUMBER(S) MSKCC-65163
CLOSING DATE: 00/80

17.0172 IMMUNOTHERAPY WITH IRRADIATED AUTOLOGOUS CANCER CELLS AND BCG FOR NONRESECTABLE CANCER

Pinsky, C. M., (212-794-7595) Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York, 10021, United States of America
PROTOCOL NUMBER(S) MSKCC-717
CLOSING DATE: 00/80

17.0173 CHEMOTHERAPY WITH HIGH-DOSE CACP AND MANNITOL DIURESIS FOR ADVANCED CANCER

Golbey, R. B., (212-794-7093) Memorial Sloan Kettering Cancer Center, 1275 York Ave., New York, New York, 10021, United States of America
PROTOCOL NUMBER(S) MSKCC-7629
CLOSING DATE: 02/80
PATIENT ACCRUAL: 0171078

17.0174 STUDIES OF IMMUNOLOGICAL STIMULANTS IN PATIENTS RECEIVING RADIATION THERAPY FOR CARCINOMA OF HEAD AND NECK, UTERINE CERVIX AND LUNG

McLaren, J. R., (414-377-9111) Emory University School of Medicine, 1365 Clifton Road, Atlanta, Georgia, 30322, United States of America
PROTOCOL NUMBER(S) GA-EU-1-CB-64061
CLOSING DATE: 06/80

17.0175 CHEMOTHERAPY WITH VM-26 OR VP-16 IN CHILDREN WITH ACUTE LEUKEMIA OR SOLID TUMORS

Rivera, G., (901-525-8381) St. Jude Childrens Research Hospital, 332 N. Lauderdale St., P.O. Box 318, Memphis, Tennessee, 38101, United States of America
PROTOCOL NUMBER(S) SJCRH-PODOPH-1
CLOSING DATE: 08/80

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  Corynebacterium Parvum-Merieux 1.0026

  Corynebacterium Parvum-unspecified 1.0096

  Cyclophosphamide 1.0001, 1.0003, 1.0004, 1.0006, 1.0007, 1.0008, 1.0015, 1.0018, 1.0019, 1.0020, 1.0021, 1.0030, 1.0031, 1.0032, 1.0034, 1.0035, 1.0036, 1.0038, 1.0041, 1.0044, 1.0045, 1.0048, 1.0050, 1.0051, 1.0052, 1.0053, 1.0054, 1.0062, 1.0066, 1.0067, 1.0070, 1.0071, 1.0072, 1.0073, 1.0074, 1.0075, 1.0076, 1.0079, 1.0080, 1.0081, 1.0082, 1.0083, 1.0084, 1.0085, 1.0088, 1.0089, 1.0090, 1.0092, 1.0093, 1.0096, 1.0097, 1.0099, 1.0100, 1.0101, 1.0103, 1.0104, 17.0001, 17.0002, 17.0003, 17.0004, 17.0008, 17.0015, 17.0016, 17.0024

  Cytosine Arabinoside 1.0031

  Dexamethasone 1.0014, 1.0017, 1.0034, 1.0069, 14.0006, 14.0007, 15.0045

  Dibromodulcitol 1.0012, 1.0013, 1.0045, 1.0046, 1.0049, 1.0097, 17.0012, 17.0016

  Diethylstilbestrol 1.0033, 17.0006

  Diglycoaldehyde 1.0029

  Dihydroxyanthracenedione 1.0039, 17.0023

  Estrogens, conjugated 1.0070

  Florinef 1.0014, 1.0069

  5-Fluorouracil 1.0001, 1.0003, 1.0004, 1.0006, 1.0007, 1.0008, 1.0015, 1.0018, 1.0019, 1.0020, 1.0021, 1.0022, 1.0025, 1.0026, 1.0030, 1.0031, 1.0032, 1.0034, 1.0035, 1.0036, 1.0038, 1.0041, 1.0044, 1.0045, 1.0048, 1.0050, 1.0051, 1.0052, 1.0053, 1.0054, 1.0062, 1.0066, 1.0067, 1.0070, 1.0072, 1.0073, 1.0075, 1.0079, 1.0080, 1.0081, 1.0082, 1.0083, 1.0084, 1.0085, 1.0088, 1.0089, 1.0090, 1.0092, 1.0093, 1.0096, 1.0097, 1.0099, 1.0101, 1.0104, 15.003 , 17.0001, 17.0002, 17.0003, 17.0004, 17.0008, 17.0015, 17.0016, 17.0024

  Fluoxymesterone 1.0004, 1.0012, 1.0015, 1.0068

  Ftorafur 1.0049, 1.0080

  Gallium Nitrate 17.0005

  Hexamethylmelamine 1.0097

  Hydrocortisone 1.0014, 1.0016, 1.0017, 1.0047, 1.0105, 1.0106

  Hyperthermia 17.0166, 17.0167

  ICRF-159 1.0013

  Interferon 1.0052, 15.0037, 15.0054, 17.0014

  Levamisole 1.0032, 1.0067, 1.0082, 1.0083, 1.0087, 1.0089, 1.0099, 1.0104, 17.0004, 17.0025

  Maytansine 17.0007

  Medroxyprogesterone Acetate 1.0076, 1.0077, 1.0078, 1.0097, 1.0102

  Megestrol Acetate 17.0006

  Melphalan 1.0025, 1.0026, 1.0027, 1.0074, 1.0101, 1.0104, 17.0010, 17.0024, 17.0025

  MER-BCG 17.0001, 17.0002

  Methotrexate 1.0003, 1.0004, 1.0006, 1.0007, 1.0008, 1.0015, 1.0018, 1.0019, 1.0020, 1.0021, 1.0030, 1.0031, 1.0036, 1.0038, 1.0041, 1.0048, 1.0049, 1.0050, 1.0051, 1.0052, 1.0053, 1.0054, 1.0062, 1.0067, 1.0070, 1.0072, 1.0073, 1.0075, 1.0079, 1.0082, 1.0083, 1.0085, 1.0088, 1.0089, 1.0090, 1.0092, 1.0093, 1.0096, 1.0097, 1.0099, 1.0101, 1.0104, 14.0006, 14.0007, 15.0045, 17.0001, 17.0002, 17.0004, 17.0008, 17.0015, 17.0016, 17.0018, 17.0024

  Methyl-GAG 1.0037, 17.0019, 17.0169

  Misonidazole 15.0011

  Mitomycin-C 1.0012, 1.0022, 1.0042, 1.0097, 17.0012

  Nonspecific Stimulants 1.0026, 1.0032, 1.0048, 1.0050, 1.0053, 1.0063, 1.0066, 1.0067, 1.0072, 1.0073, 1.0082,

1.0083, 1.0084, 1.0087, 1.0089, 1.0096, 1.0099, 1.0104, 15.0054, 17.0001, 17.0002, 17.0004, 17.0008, 17.0025
PALA 1.0005, 1.0091
PCNU 17.0022
Peptichemio 17.0010, 17.0015, 17.0020, 17.0021
cis-Platinum 1.0045, 15.0021
Poly IC 1.0063, 15.0054
Prednisolone 1.0092
Prednisone 1.0001, 1.0004, 1.0006, 1.0007, 1.0008, 1.0015, 1.0018, 1.0019, 1.0021, 1.0024, 1.0036, 1.0044, 1.0045, 1.0062, 17.0001, 17.0002, 17.0003, 17.0004, 17.0024
Procarbazine 1.0065, 1.0098
Quelamycin 1.0094
Radiation: Low-LET Co-60 gamma rays 1.0001, 1.0021, 1.0027, 1.0028, 1.0030, 1.0040, 1.0066, 1.0089, 1.0092, 1.0093, 1.0099, 15.0011, 17.0167
Radiation: Low-LET electrons 1.0040, 1.0088, 1.0093
Radiation: Low-LET Implant 1.0040, 1.0071, 1.0093
Radiation: Low-LET photons 1-4 MeV 1.0001, 1.0008, 1.0021, 1.0027, 1.0028, 1.0030, 1.0040, 1.0071, 1.0074, 1.0089, 1.0092, 1.0093, 1.0099, 1.0104, 15.0011, 15.0012, 15.0045, 17.0167
Radiation: Low-LET photons above 4 MeV 1.0001, 1.0008, 1.0021, 1.0028, 1.0030, 1.0071, 1.0089, 1.0092, 1.0093, 1.0099, 15.0011, 15.0012, 15.0045, 17.0167
Radiation: Low-LET, unspecified 1.0049, 1.0053, 1.0054, 1.0073, 14.0006, 14.0007, 17.0008, 17.0166
Retinoids 15.0051
Spirogermanium 1.0002
Streptonigrin 17.0024
Surgery 1.0001, 1.0015, 1.0016, 1.0027, 1.0036, 1.0040, 1.0053, 1.0054, 1.0066, 1.0067, 1.0071, 1.0093, 1.0099, 1.0100, 1.0101, 1.0104, 17.0003
Surgery: Ablative 1.0010, 1.0014, 1.0016, 1.0034, 1.0035, 1.0044, 1.0069, 1.0097, 1.0102, 17.0003
Tamoxifen 1.0003, 1.0011, 1.0012, 1.0014, 1.0016, 1.0017, 1.0018, 1.0019, 1.0020, 1.0025, 1.0033, 1.0035, 1.0036, 1.0047, 1.0054, 1.0062, 1.0070, 1.0081, 1.0085, 1.0090, 1.0092, 1.0093, 1.0097, 1.0103, 1.0104, 1.0106, 17.0006
Thio-TEPA 1.0004, 1.0068, 14.0006, 14.0007, 15.0045, 17.0015, 17.0024
Thymidine 15.0033
Trioxifene mesylate 1.0058
Tumor Cells/Cell Fractions 1.0053, 1.0104, 17.0011
Vinblastine 1.0004, 1.0042, 1.0055, 1.0059, 1.0062, 1.0064, 1.0068, 1.0080, 1.0081, 17.0018, 17.0021, 17.0024
Vincristine 1.0001, 1.0004, 1.0013, 1.0022, 1.0031, 1.0036, 1.0038, 1.0062, 1.0075, 1.0076, 1.0082, 1.0096, 1.0097, 17.0001, 17.0002, 17.0003, 17.0004, 17.0024
Vindesine 1.0095, 15.0039
VP-16 1.0043, 1.0057

Carcinoid
Adriamycin 15.0017, 15.0028
Cyclophosphamide 15.0017, 15.0028
5-Fluorouracil 2.0051, 2.0052, 15.0017, 15.0028
Methotrexate 15.0028
Mitomycin-C 2.0052
Radiation: Low-LET Co-60 gamma rays 2.0051, 2.0052
Radiation: Low-LET photons 1-4 MeV 2.0051, 2.0052
Radiation: Low-LET photons above 4 MeV 2.0051, 2.0052
Streptozotocin 2.0052, 15.0017, 15.0026

Cervix *see* Gynecologic Tumors

Colon *see* Gastrointestinal Tumors

Endocrine Tumors: Adrenal
Adriamycin 3.0085, 3.0096
Cortisone 3.0085
Cyclophosphamide 3.0096
Fludrocortisone 3.0085
Mitotane 3.0085, 3.0096
cis-Platinum 3.0096

Endocrine Tumors: Endocrine Pancreas
Chlorozotocin 2.0045, 2.0048
Dianhydrogalactitol 2.0048
5-Fluorouracil 2.0046, 2.0048
Hexamethylmelamine 2.0048
ICRF-159 2.0048
Maytansine 2.0048
Mitomycin-C 2.0048
Radiation: High-LET heavy ions 2.0050
Radiation: Low-LET Co-60 gamma rays 2.0046
Radiation: Low-LET photons 1-4 MeV 2.0046
Radiation: Low-LET photons above 4 MeV 2.0046
Streptozotocin 2.0048, 15.0026
beta-TGdR 2.0048

Endocrine Tumors: Thyroid
Adriamycin 12.0004, 12.0019, 12.0032
PALA 17.0157
cis-Platinum 12.0004, 12.0019, 12.0032

Esophagus *see* Gastrointestinal Tumors

Ewing's Sarcoma *see* Pediatric Solid Tumors

Gastrointestinal Tumors: Colon and Rectum
Actinomycin-D 2.0067
Adriamycin 2.0075, 17.0050
Alanosine, L- 2.0088
AMSA 2.0068, 2.0101, 15.0044, 15.0072, 17.0051
Anguidine 17.0049
Aspirin 17.0040
AZQ 2.0089, 2.0094
Baker's Antifol 2.0085, 2.0110
BCG-Connaught 2.0107, 2.0130, 17.0034
BCG-Glaxo 2.0126, 15.0056
BCG-Pasteur 2.0070, 2.0090
BCG-Tice 2.0074, 2.0105, 2.0106
BCG-Unspecified 2.0115, 2.0131, 2.0134
Bleomycin 2.0075
CCNU 2.0067
Chlorozotocin 2.0068

Citrovorum Factor 2.0069
Corynebacterium Parvum-Burroughs 17.0040, 17.0047
Corynebacterium Parvum-unspecified 2.0114
Cyclophosphamide 2.0068
Dihydroxyanthracenedione 2.0080, 2.0096
DTIC 17.0031
Floxuridine 2.0090, 2.0095, 17.0040
5-Fluorouracil 2.0066, 2.0069, 2.0070, 2.0071, 2.0072, 2.0074, 2.0075, 2.0077, 2.0081, 2.0083, 2.0084, 2.0085, 2.0091, 2.0095, 2.0097, 2.0099, 2.0104, 2.0105, 2.0106, 2.0108, 2.0109, 2.0110, 2.0111, 2.0112, 2.0113, 2.0114, 2.0116, 2.0119, 2.0126, 2.0130, 2.0131, 15.0033, 15.0053, 15.0056, 17.0031, 17.0033, 17.0034, 17.0035, 17.0036, 17.0041, 17.0042, 17.0043, 17.0044, 17.0045, 17.0048, 17.0053
Freund's Complete Adjuvant 2.0104
Ftorafur 2.0085, 2.0091, 2.0133, 2.0134
Gallium Nitrate 2.0079
Hydroxyurea 2.0066, 17.0031, 17.0044
Hyperthermia 17.0166, 17.0167
ICRF-159 2.0067, 2.0085, 2.0110, 17.0031, 17.0050
ICRF-187 2.0102
Indicine-N-oxide 17.0038
Isotopic Therapy 15.0058
Levamisole 2.0111, 2.0116, 2.0118, 2.0132, 2.0133
Melphalan 2.0067
MER-BCG 2.0119, 17.0037, 17.0043
Methotrexate 2.0067, 2.0068, 2.0069
Methyl-CCNU 2.0066, 2.0070, 2.0071, 2.0072, 2.0084, 2.0085, 2.0097, 2.0105, 2.0106, 2.0110, 2.0112, 2.0113, 2.0114, 2.0130, 17.0031, 17.0034, 17.0036, 17.0042, 17.0043, 17.0053
Methyl-GAG 2.0068, 2.0078, 17.0169
Misonidazole 15.0011
Mitomycin-C 2.0069, 2.0075, 2.0081, 2.0090, 2.0095, 2.0133, 15.0056, 17.0031, 17.0040
Nonspecific Stimulants 2.0070, 2.0074, 2.0090, 2.0105, 2.0106, 2.0107, 2.0111, 2.0114, 2.0115, 2.0116, 2.0118, 2.0119, 2.0126, 2.0130, 2.0131, 2.0132, 2.0133, 2.0134, 15.0056, 17.0034, 17.0037, 17.0040, 17.0042, 17.0043, 17.0047
OK-432 2.0134
PALA 2.0087, 2.0092, 17.0041
PCNU 2.0065, 2.0093, 2.0103
Piperazinedione 2.0067
PSK 2.0134
Radiation: High-LET pions 2.0073
Radiation: Low-LET Co-60 gamma rays 2.0071, 2.0072, 2.0073, 2.0081, 2.0083, 2.0100, 2.0112, 2.0117, 2.0119, 15.0011, 17.0030, 17.0032, 17.0036, 17.0037, 17.0046, 17.0048, 17.0167
Radiation: Low-LET photons 1-4 MeV 2.0071, 2.0072, 2.0081, 2.0083, 2.0098, 2.0100, 2.0112, 2.0117, 2.0119, 15.0011, 17.0030, 17.0032, 17.0036, 17.0037, 17.0046, 17.0048, 17.0167
Radiation: Low-LET photons above 4 MeV 2.0071, 2.0072, 2.0073, 2.0081, 2.0083, 2.0100, 2.0117, 2.0119, 15.0011, 17.0030, 17.0032, 17.0036, 17.0037, 17.0046, 17.0167
Radiation: Low-LET, unspecified 2.0090, 15.0056, 17.0166
Spirogermanium 2.0064
Streptonigrin 17.0045
Streptozotocin 2.0084, 2.0097
Surgery 2.0073, 2.0098, 2.0100, 2.0115, 2.0117, 2.0120, 2.0131, 2.0132, 2.0134, 17.0046
Tamoxifen 2.0076
Thio-TEPA 17.0045
Thioguanine 2.0082, 17.0033, 17.0039
Thymidine 15.0033
Tumor Cells/Cell Fractions 2.0104, 2.0115
Urokinase 2.0120
Vinblastine 17.0045
Vincristine 2.0068, 2.0070, 2.0071, 2.0084, 2.0085, 2.0097, 2.0113, 2.0114
Vindesine 2.0095, 17.0053
Virus/Viral Substances 2.0108, 2.0109
Vitamin A 15.0056
Vitamin C 2.0086
VP-16 15.0038
Warfarin 2.0120
Yoshi-864 2.0067

Gastrointestinal Tumors: Esophagus
Adriamycin 2.0010, 2.0123, 2.0127
BCG-Tice 2.0012, 2.0013
Bleomycin 2.0001, 2.0006, 2.0010, 2.0011
Citrovorum Factor 2.0014
Cyclophosphamide 2.0009
Dibromodulcitol 15.0036
5-Fluorouracil 2.0123, 2.0127
Hyperthermia 17.0166, 17.0167
Levamisole 2.0132
MER-BCG 2.0014
Methotrexate 2.0001, 2.0006, 2.0014, 2.0016
Methyl-GAG 2.0001, 2.0017, 17.0169
Misonidazole 2.0005
Mitomycin-C 2.0002, 2.0009, 2.0123, 2.0127
Nonspecific Stimulants 2.0012, 2.0013, 2.0014, 2.0132
cis-Platinum 2.0001, 2.0002, 2.0006, 2.0007, 2.0008, 2.0010, 2.0011, 2.0014
Radiation: High-LET heavy ions 2.0003, 15.0005
Radiation: High-LET neutrons 2.0004
Radiation: Low-LET Co-60 gamma rays 2.0004, 2.0005, 2.0015, 2.0016, 17.0167
Radiation: Low-LET photons 1-4 MeV 2.0004, 2.0005, 2.0006, 2.0015, 2.0016, 17.0167
Radiation: Low-LET photons above 4 MeV 2.0005, 2.0006, 2.0015, 2.0016, 17.0167
Radiation: Low-LET, unspecified 2.0010, 2.0012, 2.0013, 2.0014, 17.0166
Radiation: Mixed High/Low LET 2.0004
Surgery 2.0007, 2.0014, 2.0015, 2.0132

Vindesine 2.0011

Gastrointestinal Tumors: Gall Bladder

Adriamycin 2.0128
5-Fluorouracil 2.0128
Methyl-CCNU 2.0128
Streptozotocin 2.0128
Vinblastine 2.0128

Gastrointestinal Tumors: Liver

Adriamycin 2.0053, 2.0054, 2.0055, 2.0056, 2.0057, 2.0058, 2.0060, 2.0062, 2.0128, 2.0129, 10.0014, 10.0033
AMSA 2.0053, 2.0059, 15.0004
BCG-Glaxo 2.0126
BCG-Tice 2.0125
BCG-Unspecified 2.0134
BCNU 2.0062
Bleomycin 2.0058
Citrovorum Factor 2.0055
Corynebacterium Parvum-Burroughs 2.0062
Cyclophosphamide 10.0033
Dichloromethotrexate 14.0008
DTIC 10.0033
Floxuridine 2.0060
5-Fluorouracil 2.0054, 2.0055, 2.0056, 2.0057, 2.0060, 2.0062, 2.0126, 2.0128, 17.0048
Ftorafur 2.0134
Isotopic Therapy 2.0057, 15.0058
Methotrexate 2.0055
Methyl-CCNU 2.0128
Mitomycin-C 2.0056
Neocarzinostatin 2.0053, 2.0061, 17.0164, 17.0170
Nonspecific Stimulants 2.0062, 2.0125, 2.0126, 2.0134
OK-432 2.0134
PSK 2.0134
Radiation: Low-LET Co-60 gamma rays 2.0054, 2.0055, 2.0056, 2.0057, 2.0129, 17.0048
Radiation: Low-LET photons 1-4 MeV 2.0054, 2.0055, 2.0056, 2.0057, 2.0129, 17.0048
Radiation: Low-LET photons above 4 MeV 2.0054, 2.0055, 2.0056, 2.0129
Streptozotocin 2.0060, 2.0128
Surgery 2.0134
Vinblastine 2.0128
VP-16 2.0061, 2.0063, 15.0038

Gastrointestinal Tumors: Pancreas

AAFC 14.0009
Adriamycin 2.0039, 2.0040, 2.0041, 2.0042, 2.0047, 2.0049, 2.0127, 2.0128, 2.0129, 15.0069, 17.0050, 17.0052
AMSA 2.0121, 15.0072, 17.0051
Anguidine 17.0049
BCG-Glaxo 2.0126
BCG-Tice 2.0125
BCG-Unspecified 2.0131, 2.0134
BCNU 2.0042
Chlorozotocin 2.0041, 2.0048, 2.0049, 15.0003, 15.0049
Dianhydrogalactitol 2.0048, 2.0049
5-Fluorouracil 2.0039, 2.0041, 2.0042, 2.0043, 2.0046, 2.0047, 2.0048, 2.0049, 2.0051, 2.0052, 2.0126, 2.0127, 2.0128, 2.0131, 15.0069, 17.0029, 17.0048, 17.0052, 17.0053
Ftorafur 2.0042, 2.0134
Hexamethylmelamine 2.0048, 2.0049
Hyperthermia 17.0166, 17.0167
ICRF-159 2.0048, 17.0050
Maytansine 2.0048, 2.0049
Methyl-CCNU 2.0040, 2.0128, 17.0053
Methyl-GAG 17.0169
Mitomycin-C 2.0039, 2.0048, 2.0049, 2.0052, 2.0127, 17.0029
Neocarzinostatin 17.0164
Nonspecific Stimulants 2.0125, 2.0126, 2.0131, 2.0134
OK-432 2.0134
PALA 2.0040
cis-Platinum 2.0122, 15.0069, 17.0052
PSK 2.0134
Radiation: High-LET heavy ions 2.0043, 15.0005
Radiation: High-LET neutrons 2.0044
Radiation: Low-LET Co-60 gamma rays 2.0046, 2.0051, 2.0052, 2.0129, 17.0048, 17.0167
Radiation: Low-LET photons 1-4 MeV 2.0046, 2.0047, 2.0051, 2.0052, 2.0129, 17.0048, 17.0167
Radiation: Low-LET photons above 4 MeV 2.0046, 2.0047, 2.0051, 2.0052, 2.0129, 17.0167
Radiation: Low-LET, unspecified 2.0044, 17.0166
Radiation: Mixed High/Low LET 2.0044
Streptozotocin 2.0039, 2.0040, 2.0041, 2.0048, 2.0049, 2.0052, 2.0128, 17.0029
Surgery 2.0131, 2.0134
beta-TGdR 2.0048
Vinblastine 2.0128
Vindesine 17.0053

Gastrointestinal Tumors: Stomach

Adriamycin 2.0018, 2.0019, 2.0021, 2.0022, 2.0023, 2.0024, 2.0025, 2.0026, 2.0027, 2.0028, 2.0030, 2.0033, 2.0034, 2.0123, 2.0127, 2.0129, 15.0069, 17.0050, 17.0052
AMSA 2.0121, 15.0072, 17.0051
Anguidine 17.0049
Bacteria/Bacterial Substances 2.0036, 2.0037
Baker's Antifol 2.0029
BCG-Connaught 2.0130
BCG-Tice 2.0125
BCG-Unspecified 2.0131, 2.0134
BCNU 2.0023
Chlorozotocin 2.0025
Citrovorum Factor 2.0029
5-Fluorouracil 2.0018, 2.0019, 2.0021, 2.0022, 2.0023, 2.0024, 2.0025, 2.0026, 2.0027, 2.0028, 2.0030, 2.0033, 2.0034, 2.0123, 2.0127, 2.0130, 2.0131, 15.0069, 17.0026, 17.0027, 17.0028, 17.0048, 17.0052, 17.0053

Ftorafur 2.0023, 2.0036, 2.0037, 2.0133, 2.0134
ICRF-159 2.0027, 2.0029, 2.0031, 17.0050
Levamisole 2.0132, 2.0133
Methotrexate 2.0029
Methyl-CCNU 2.0022, 2.0026, 2.0027, 2.0028, 2.0034, 2.0130, 17.0026, 17.0027, 17.0028, 17.0053
Misonidazole 2.0032
Mitomycin-C 2.0018, 2.0019, 2.0022, 2.0023, 2.0024, 2.0025, 2.0027, 2.0028, 2.0033, 2.0036, 2.0123, 2.0127, 2.0133
Neocarzinostatin 17.0164
Nonspecific Stimulants 2.0125, 2.0130, 2.0131, 2.0132, 2.0133, 2.0134
OK-432 2.0036, 2.0037, 2.0134
cis-Platinum 2.0020, 2.0021, 2.0035, 2.0122, 15.0069, 17.0052
PSK 2.0134
Radiation: High-LET heavy ions 15.0005
Radiation: Low-LET Co-60 gamma rays 2.0129, 17.0048
Radiation: Low-LET electrons 2.0032
Radiation: Low-LET photons 1-4 MeV 2.0129, 17.0048
Radiation: Low-LET photons above 4 MeV 2.0129
Radiation: Low-LET, unspecified 2.0032
Surgery 2.0019, 2.0032, 2.0036, 2.0131, 2.0132, 2.0134, 17.0028
Vincristine 2.0025
Vindesine 17.0053
VP-16 2.0038

Gastrointestinal Tumors: general
Adriamycin 15.0017
AMSA 17.0051
BCG-Glaxo 2.0126, 15.0056
BCG-Unspecified 2.0131
Chlorozotocin 15.0003
Cyclophosphamide 15.0017
5-Fluorouracil 2.0124, 2.0126, 2.0131, 15.0017, 15.0053, 15.0056
Methyl-CCNU 2.0124
Misonidazole 15.0010
Mitomycin-C 15.0056
Nonspecific Stimulants 2.0126, 2.0131, 15.0056
cis-Platinum 15.0021
Radiation: Low-LET Co-60 gamma rays 15.0010
Radiation: Low-LET photons 1-4 MeV 15.0010
Radiation: Low-LET photons above 4 MeV 15.0010
Radiation: Low-LET, unspecified 15.0056
Streptozotocin 15.0017
Surgery 2.0131
Vincristine 2.0124
Vitamin A 15.0056

Genitourinary Tumors: Bladder
Adriamycin 3.0002, 3.0007, 3.0008, 3.0009, 3.0010, 3.0013, 3.0018, 3.0020, 3.0021, 3.0022, 3.0024, 3.0086, 3.0094, 3.0095, 15.0019
AMSA 3.0010, 3.0091
AZQ 3.0093
BCG-Pasteur 3.0017
BCG-Tice 3.0016
BCG-Unspecified 3.0015
Bleomycin 15.0027
Cyclophosphamide 3.0002, 3.0007, 3.0008, 3.0009, 3.0010, 3.0086, 3.0094, 3.0095
Epodyl 3.0022
5-Fluorouracil 3.0009, 3.0021, 3.0024
Gallium Nitrate 3.0090
Hexamethylmelamine 3.0009, 3.0011, 3.0087
Hyperthermia 17.0166, 17.0167
Levamisole 3.0026, 3.0027
Methotrexate 15.0027
Misonidazole 3.0003, 17.0054
Mitomycin-C 3.0012, 3.0014
Neocarzinostatin 17.0164, 17.0170
Nonspecific Stimulants 3.0015, 3.0016, 3.0017, 3.0026, 3.0027, 15.0027
Non-tumor Cells/Cell Fractions 3.0025
cis-Platinum 3.0001, 3.0002, 3.0003, 3.0007, 3.0008, 3.0010, 3.0020, 3.0086, 3.0087, 3.0088, 3.0092, 3.0094, 3.0095, 15.0019, 15.0027
Radiation: High-LET neutrons 3.0004
Radiation: High-LET pions 3.0006
Radiation: Low-LET Co-60 gamma rays 3.0004, 3.0005, 3.0006, 3.0021, 15.0006, 17.0054, 17.0167
Radiation: Low-LET electrons 3.0005
Radiation: Low-LET photons 1-4 MeV 3.0001, 3.0005, 3.0006, 3.0021, 15.0006, 17.0054, 17.0167
Radiation: Low-LET photons above 4 MeV 3.0001, 3.0003, 3.0004, 3.0005, 3.0006, 3.0021, 3.0025, 17.0054, 17.0167
Radiation: Low-LET, unspecified 3.0007, 3.0024, 17.0166
Radiation: Mixed High/Low LET 3.0004
Surgery 3.0001, 3.0003, 3.0004, 3.0005, 3.0007, 3.0015, 3.0017, 3.0019, 3.0020, 3.0021, 3.0022, 3.0086
Thio-TEPA 3.0014, 3.0020
Thymosin 15.0027
Vincristine 3.0023
Vitamin B 3.0019
VM-26 3.0026, 3.0027
VP-16 3.0088, 3.0089, 3.0092

Genitourinary Tumors: Kidney
Actinomycin-D 11.0001, 17.0055, 17.0145
Adriamycin 3.0086, 3.0094, 3.0095, 11.0001, 15.0019
AMSA 3.0091, 15.0004, 15.0072, 17.0055
AZQ 3.0093
Baker's Antifol 17.0055
BCG-Tice 15.0059
BCG-Unspecified 3.0038
CCNU 3.0028, 17.0055
Citrovorum Factor 15.0071

CL-216,942 3.0034
Cyclophosphamide 3.0086, 3.0094, 3.0095
DDMP 15.0071
Dihydroxyanthracenedione 3.0031
Estracyt 3.0036
Gallium Nitrate 3.0090
Hexamethylmelamine 3.0087
Hydroxyurea 3.0028
Indicine-N-oxide 17.0055
Levamisole 3.0040
Medroxyprogesterone Acetate 3.0028, 3.0029, 3.0032, 3.0035, 17.0056
Methyl-GAG 3.0030, 3.0033, 3.0041, 17.0169
Neocarzinostatin 17.0164, 17.0170
Nonspecific Stimulants 3.0038, 3.0040, 15.0059
PALA 17.0055
cis-Platinum 3.0086, 3.0087, 3.0088, 3.0094, 3.0095, 15.0019
Progesterone 3.0039
Radiation: Low-LET Co-60 gamma rays 17.0145
Radiation: Low-LET photons 1-4 MeV 17.0145
Radiation: Low-LET, unspecified 11.0001
Surgery 3.0029, 3.0035, 3.0038, 3.0086, 11.0001
Tamoxifen 3.0032
Tumor Cells/Cell Fractions 3.0038, 3.0039
Vinblastine 3.0028, 17.0055
Vincristine 11.0001, 17.0145
Vindesine 3.0037
VP-16 3.0088
Yoshi-864 17.0056

Genitourinary Tumors: Prostate
Adriamycin 3.0044, 3.0045, 3.0058, 3.0060, 3.0061, 15.0019
AMSA 3.0062, 3.0091
AZQ 3.0093
BCG-Tice 3.0063, 15.0059
Bleomycin 15.0027
Cyclophosphamide 3.0046, 3.0049, 3.0050, 3.0051, 3.0055, 3.0058, 3.0061, 17.0058
Cyproterone Acetate 3.0065
Diethylstilbestrol 3.0042, 3.0044, 3.0045, 3.0049, 3.0050, 3.0052, 3.0055, 3.0064, 3.0065, 3.0066, 17.0058, 17.0060
Dihydroxyanthracenedione 3.0056
Estracyt 3.0046, 3.0047, 3.0048, 3.0049, 3.0050, 3.0051, 3.0066, 17.0058
5-Fluorouracil 3.0049, 3.0060, 3.0061
Gallium Nitrate 3.0090
Levamisole 3.0042, 17.0060
Medroxyprogesterone Acetate 3.0065
Methotrexate 3.0047, 15.0027
Mitomycin-C 3.0060
Nitrogen Mustard 3.0061
Nonspecific Stimulants 3.0042, 3.0063, 15.0027, 15.0059, 17.0060
cis-Platinum 3.0043, 3.0044, 3.0047, 3.0048, 3.0058, 3.0061, 15.0019, 15.0027
Radiation: High-LET neutrons 3.0053
Radiation: Low-LET Co-60 gamma rays 3.0052, 3.0053, 3.0054, 3.0064
Radiation: Low-LET photons 1-4 MeV 3.0046, 3.0052, 3.0053, 3.0054, 3.0064, 15.0012
Radiation: Low-LET photons above 4 MeV 3.0046, 3.0053, 3.0064, 15.0012
Radiation: Mixed High/Low LET 3.0053
Stilphostrol 3.0052
Surgery: Ablative 3.0049, 3.0061, 3.0064, 17.0058
Tamoxifen 3.0057, 3.0059, 17.0057, 17.0059
Thymosin 15.0027
Vindesine 3.0067
VP-16 3.0089

Genitourinary Tumors: Testis
Actinomycin-D 3.0072, 3.0073, 3.0078, 3.0079, 3.0081, 17.0061, 17.0062
Adriamycin 3.0070, 3.0071, 3.0072, 3.0077, 15.0019, 17.0061, 17.0062
AMSA 3.0091, 15.0072
AZQ 3.0093
BCG-Tice 15.0059
Bleomycin 3.0069, 3.0070, 3.0071, 3.0072, 3.0073, 3.0074, 3.0075, 3.0076, 3.0078, 3.0079, 3.0080, 3.0081, 3.0082, 15.0027, 17.0061, 17.0062
Bone Marrow Therapy: Autologous 3.0077
Cyclophosphamide 3.0072, 3.0073, 3.0077, 3.0078, 3.0079, 17.0061, 17.0062
Diglycoaldehyde 17.0165
Gallium Nitrate 3.0090
Lithium Carbonate 3.0069
Methotrexate 15.0027
Nonspecific Stimulants 15.0027, 15.0059
cis-Platinum 3.0069, 3.0070, 3.0071, 3.0072, 3.0073, 3.0074, 3.0076, 3.0078, 3.0079, 3.0080, 3.0081, 3.0082, 3.0083, 15.0019, 15.0027, 17.0061, 17.0062
Radiation: Low-LET electrons 3.0068
Radiation: Low-LET photons 1-4 MeV 3.0068
Retinoids 15.0051
Surgery 3.0068, 3.0072, 3.0073, 3.0074, 3.0078, 3.0079
Surgery: Ablative 3.0068, 3.0073, 3.0074
Thymosin 15.0027
Vinblastine 3.0069, 3.0071, 3.0072, 3.0073, 3.0074, 3.0075, 3.0076, 3.0078, 3.0079, 3.0080, 3.0081, 3.0082, 3.0083, 17.0061, 17.0062
Vincristine 17.0061
VP-16 3.0070, 3.0077, 3.0080

Genitourinary Tumors: general
Adriamycin 3.0084
AMSA 3.0091
BCNU 15.0023
Cyclophosphamide 3.0084
Furosemide 3.0084

cis-Platinum 3.0084, 3.0092
Thioguanine 15.0023
VM-26 3.0084
VP-16 3.0092

Genitourinary Tumors: other
Adriamycin 3.0086
BCG-Unspecified 15.0070
Bleomycin 15.0070
Cyclophosphamide 3.0086
Nonspecific Stimulants 15.0070
cis-Platinum 3.0086, 3.0088, 15.0070
Surgery 3.0086, 15.0070
VP-16 3.0088

Gynecologic Tumors: Cervix
Adriamycin 4.0007, 4.0014, 4.0015, 4.0016, 15.0019
AMSA 4.0082, 4.0083, 15.0072
Baker's Antifol 4.0073
BCG-Tice 17.0174
BCG-Unspecified 15.0070
Bleomycin 4.0008, 4.0013, 4.0014, 4.0018, 4.0020, 4.0021, 15.0070
Corynebacterium Parvum-Burroughs 4.0002, 4.0022, 4.0023
Corynebacterium Parvum-unspecified 4.0015
Cyclophosphamide 4.0006, 4.0014, 4.0016, 4.0018, 4.0019
Cytosine Arabinoside 4.0019
Dianhydrogalactitol 4.0001, 4.0072
5-Fluorouracil 4.0014
Hexamethylmelamine 4.0016, 17.0168
ICRF-159 4.0074
Levamisole 17.0174
Maytansine 4.0075
Misonidazole 4.0010, 4.0012, 4.0017, 15.0010
Mitomycin-C 4.0008, 4.0013, 4.0014, 4.0018, 4.0021
Nonspecific Stimulants 4.0002, 4.0015, 4.0022, 4.0023, 15.0070, 17.0174
cis-Platinum 4.0001, 4.0005, 4.0006, 4.0007, 4.0013, 4.0014, 4.0019, 4.0020, 4.0021, 4.0070, 15.0019, 15.0070
Radiation: High-LET neutrons 4.0009, 4.0015
Radiation: Low-LET Co-60 gamma rays 4.0002, 4.0009, 4.0010, 4.0011, 4.0012, 4.0022, 4.0023, 15.0006, 15.0010
Radiation: Low-LET Implant 4.0002, 4.0010, 4.0012, 4.0015, 4.0021, 4.0022, 4.0023
Radiation: Low-LET photons 1-4 MeV 4.0002, 4.0010, 4.0011, 4.0012, 15.0006, 15.0010
Radiation: Low-LET photons above 4 MeV 4.0002, 4.0009, 4.0010, 4.0011, 4.0012, 4.0015, 15.0010
Radiation: Low-LET, unspecified 4.0017, 4.0021, 4.0084
Surgery 4.0003, 4.0004, 4.0021, 15.0070
Vincristine 4.0013, 4.0014
Virus/Viral Substances 4.0084
VP-16 4.0071
Yoshi-864 4.0085

Gynecologic Tumors: Ovary
Actinomycin-D 4.0030, 4.0031, 4.0044, 15.0002, 17.0065, 17.0066
Adriamycin 4.0024, 4.0025, 4.0028, 4.0033, 4.0034, 4.0035, 4.0036, 4.0037, 4.0038, 4.0039, 4.0040, 4.0041, 4.0044, 4.0045, 4.0049, 4.0050, 4.0051, 4.0058, 4.0081, 15.0002, 15.0019, 17.0064, 17.0067, 17.0071
AMSA 4.0052, 4.0082, 4.0083, 15.0004, 15.0044
Baker's Antifol 4.0073
BCG-Connaught 4.0036, 17.0071
BCG-Pasteur 17.0071
BCG-Tice 15.0059, 17.0063
BCG-Unspecified 4.0046, 4.0047
Bleomycin 4.0031, 4.0054, 15.0002
Chlorambucil 4.0041, 4.0056, 4.0057, 17.0065
Chlorozotocin 15.0049
Citrovorum Factor 4.0044
Corynebacterium Parvum-Burroughs 4.0024, 4.0027, 4.0044
Cyclophosphamide 4.0025, 4.0030, 4.0031, 4.0033, 4.0034, 4.0035, 4.0036, 4.0037, 4.0038, 4.0039, 4.0040, 4.0041, 4.0044, 4.0045, 4.0051, 4.0058, 4.0081, 15.0002, 17.0064, 17.0066, 17.0071
Dianhydrogalactitol 4.0072
5-Fluorouracil 2.0051, 4.0044, 4.0051, 15.0053
Hexamethylmelamine 4.0024, 4.0025, 4.0026, 4.0038, 4.0039, 4.0040, 4.0049, 4.0050, 4.0051, 4.0057, 4.0058, 17.0064, 17.0168
ICRF-159 4.0074
Isoniazid 17.0063
Isotopic Therapy 4.0043, 4.0048
Levamisole 4.0032
Maytansine 4.0075
Medroxyprogesterone Acetate 4.0056
Melphalan 4.0027, 4.0029, 4.0032, 4.0039, 4.0040, 4.0042, 4.0043, 4.0046, 4.0047, 4.0048, 4.0049, 4.0050, 4.0053, 17.0063, 17.0064
Methotrexate 4.0037, 4.0044, 4.0051, 17.0065
Misonidazole 15.0010
Neocarzinostatin 17.0164
Nonspecific Stimulants 4.0024, 4.0027, 4.0032, 4.0036, 4.0044, 4.0046, 4.0047, 15.0059, 17.0063, 17.0071
Non-tumor Cells/Cell Fractions 4.0059
PALA 4.0055
Phosphorus-32 4.0029
cis-Platinum 4.0024, 4.0025, 4.0026, 4.0031, 4.0033, 4.0035, 4.0036, 4.0037, 4.0038, 4.0039, 4.0040, 4.0041, 4.0045, 4.0049, 4.0050, 4.0051, 4.0058, 4.0070, 4.0081, 15.0002, 15.0019, 17.0064
Radiation: Low-LET Co-60 gamma rays 2.0051, 4.0025, 4.0046, 4.0048, 4.0053, 15.0002, 15.0010
Radiation: Low-LET Implant 4.0029
Radiation: Low-LET photons 1-4 MeV 2.0051, 4.0025, 4.0046, 4.0048, 4.0053, 15.0002, 15.0010

Radiation: Low-LET photons above 4 MeV 2.0051, 4.0025, 4.0034, 4.0046, 4.0048, 4.0053, 15.0002, 15.0010
Radiation: Low-LET, unspecified 17.0066
Retinoids 15.0051
Surgery 4.0025, 4.0028, 4.0034, 4.0035, 4.0039, 4.0041, 4.0049, 4.0051, 15.0002
Vinblastine 4.0031, 15.0002
Vincristine 4.0030, 4.0031, 4.0044, 17.0066
VP-16 4.0037, 4.0071, 17.0067
Yoshi-864 4.0085

Gynecologic Tumors: Uterus
Adriamycin 4.0060, 4.0061, 4.0062, 4.0063, 4.0065, 4.0066, 4.0081, 10.0033, 17.0071, 17.0143
AMSA 4.0082, 4.0083, 15.0072
BCG-Connaught 17.0071
BCG-Pasteur 17.0071
BCG-Tice 15.0059
Corynebacterium Parvum-Burroughs 17.0143
Cyclophosphamide 4.0062, 4.0063, 4.0065, 4.0066, 4.0081, 10.0033, 17.0071, 17.0143
Dianhydrogalactitol 4.0072
DTIC 10.0033
Estrogens, conjugated 4.0066
5-Fluorouracil 4.0066, 17.0070
Medroxyprogesterone Acetate 4.0063, 4.0068, 17.0068, 17.0070
Megestrol Acetate 4.0066
Melphalan 17.0070
Methotrexate 17.0143
Misonidazole 15.0010
Neocarzinostatin 17.0164
Nonspecific Stimulants 15.0059, 17.0071, 17.0143
cis-Platinum 4.0065, 4.0070, 4.0081
Progesterone 17.0068
Radiation: Low-LET Co-60 gamma rays 4.0061, 4.0064, 15.0010
Radiation: Low-LET Implant 4.0064
Radiation: Low-LET photons 1-4 MeV 4.0061, 4.0064, 15.0010
Radiation: Low-LET photons above 4 MeV 4.0061, 4.0064, 15.0010
Surgery 4.0061, 4.0064
Tamoxifen 4.0067, 17.0069
VP-16 4.0071
Yoshi-864 4.0085

Gynecologic Tumors: Vagina
Adriamycin 4.0014
AMSA 4.0082
Bleomycin 4.0014, 4.0069
Cyclophosphamide 4.0014
5-Fluorouracil 4.0014
Mitomycin-C 4.0014
cis-Platinum 4.0014, 4.0069, 4.0070
Radiation: Low-LET Co-60 gamma rays 4.0080
Radiation: Low-LET Implant 4.0069
Radiation: Low-LET photons 1-4 MeV 4.0080
Radiation: Low-LET photons above 4 MeV 4.0069, 4.0080
Surgery 4.0079, 4.0080
Vincristine 4.0014
VP-16 4.0071

Gynecologic Tumors: Vulva
Adriamycin 4.0014
AMSA 4.0082
Bleomycin 4.0014, 4.0069
Cyclophosphamide 4.0014
Dianhydrogalactitol 4.0072
5-Fluorouracil 4.0014
Mitomycin-C 4.0014
cis-Platinum 4.0014, 4.0069, 4.0070
Radiation: Low-LET Co-60 gamma rays 4.0080
Radiation: Low-LET Implant 4.0069
Radiation: Low-LET photons 1-4 MeV 4.0080
Radiation: Low-LET photons above 4 MeV 4.0069, 4.0080
Radiation: Low-LET, unspecified 4.0084
Surgery 4.0079, 4.0080
Vincristine 4.0014
Virus/Viral Substances 4.0084

Gynecologic Tumors: general
AMSA 4.0076
Baker's Antifol 4.0073
Chlorozotocin 4.0078
Dianhydrogalactitol 4.0072
ICRF-159 4.0074
Maytansine 4.0075
cis-Platinum 4.0070
VP-16 4.0071
Yoshi-864 4.0077

Head and Neck Tumors
AAFC 14.0009
Adriamycin 12.0024, 12.0050, 15.0025, 17.0156
AMSA 12.0026, 12.0036, 15.0072
AZQ 12.0029
BCG-Connaught 12.0031
BCG-Pasteur 12.0047, 12.0054
BCG-Tice 12.0039, 12.0041, 15.0057, 17.0174
BCG-Unspecified 12.0059, 15.0070
Bleomycin 12.0001, 12.0003, 12.0006, 12.0020, 12.0021, 12.0022, 12.0023, 12.0027, 12.0030, 12.0031, 12.0035, 12.0044, 12.0045, 12.0046, 12.0050, 12.0051, 12.0052, 12.0057, 15.0027, 15.0070, 17.0154, 17.0158
Citrovorum Factor 12.0007, 12.0021, 12.0022, 12.0035, 12.0042, 12.0057, 15.0071
Corynebacterium Parvum-Burroughs 17.0153, 17.0154
Cyclophosphamide 8.0039, 12.0001, 12.0024, 12.0028, 12.0031, 12.0035, 12.0044, 12.0045, 12.0049, 15.0025, 17.0156
Cytosine Arabinoside 8.0039

- DDMP 15.0071
- Dibromodulcitol 12.0018, 15.0036
- Dinitrofluorobenzene 12.0040
- 5-Fluorouracil 12.0001, 12.0024, 12.0031, 12.0035
- Furosemide 12.0052
- Gallium Nitrate 12.0025
- Hydroxyurea 12.0003
- Hyperthermia 17.0166, 17.0167
- Isoniazid 12.0041
- Levamisole 12.0034, 17.0174
- Maytansine 17.0156
- MER-BCG 12.0042
- 6-Mercaptopurine 8.0039
- Methotrexate 8.0039, 12.0001, 12.0003, 12.0006, 12.0007, 12.0020, 12.0021, 12.0022, 12.0027, 12.0031, 12.0035, 12.0037, 12.0038, 12.0041, 12.0042, 12.0044, 12.0045, 12.0051, 12.0052, 12.0055, 12.0057, 12.0058, 12.0059, 15.0027, 17.0153, 17.0154, 17.0158
- Methyl-GAG 12.0005, 17.0169
- Misonidazole 12.0010, 12.0013, 12.0017
- Nonspecific Stimulants 12.0031, 12.0034, 12.0039, 12.0040, 12.0041, 12.0042, 12.0047, 12.0054, 12.0059, 15.0027, 15.0057, 15.0070, 17.0153, 17.0154, 17.0174
- PALA 12.0005, 17.0157
- PCNU 12.0033
- cis-Platinum 12.0003, 12.0007, 12.0016, 12.0020, 12.0021, 12.0022, 12.0023, 12.0027, 12.0028, 12.0030, 12.0035, 12.0037, 12.0038, 12.0042, 12.0043, 12.0044, 12.0045, 12.0046, 12.0052, 12.0055, 13.0018, 15.0021, 15.0025, 15.0027, 15.0070, 17.0154, 17.0156
- Prednisone 8.0039
- Radiation: High-LET neutrons 12.0008, 12.0057
- Radiation: High-LET pions 12.0012
- Radiation: Low-LET Co-60 gamma rays 8.0039, 12.0006, 12.0008, 12.0009, 12.0010, 12.0011, 12.0012, 12.0013, 12.0014, 12.0015, 12.0017, 12.0021, 12.0022, 12.0023, 12.0027, 12.0030, 12.0037, 12.0042, 12.0046, 12.0048, 12.0049, 12.0051, 12.0056, 12.0057, 12.0058, 15.0006, 17.0158, 17.0167
- Radiation: Low-LET electrons 12.0014, 12.0046
- Radiation: Low-LET Implant 12.0010, 12.0046
- Radiation: Low-LET photons 1-4 MeV 8.0039, 12.0009, 12.0010, 12.0012, 12.0013, 12.0014, 12.0015, 12.0017, 12.0021, 12.0022, 12.0023, 12.0027, 12.0030, 12.0037, 12.0046, 12.0048, 12.0049, 12.0051, 15.0006, 17.0158, 17.0167
- Radiation: Low-LET photons above 4 MeV 8.0039, 12.0006, 12.0008, 12.0009, 12.0010, 12.0011, 12.0012, 12.0013, 12.0014, 12.0015, 12.0017, 12.0023, 12.0027, 12.0030, 12.0037, 12.0046, 12.0048, 12.0049, 12.0051, 17.0158, 17.0167
- Radiation: Low-LET, unspecified 12.0035, 12.0039, 12.0041, 12.0045, 17.0155, 17.0166
- Radiation: Mixed High/Low LET 12.0008
- Surgery 12.0008, 12.0012, 12.0014, 12.0021, 12.0022, 12.0023, 12.0027, 12.0030, 12.0034, 12.0035, 12.0037, 12.0041, 12.0042, 12.0045, 12.0051, 15.0070, 17.0153, 17.0155, 17.0158
- Thiazolidine carboxylic acid 15.0073
- Thymosin 15.0027
- Vinblastine 12.0020, 12.0050, 17.0158
- Vincristine 8.0039, 12.0023, 12.0027, 12.0044, 12.0045, 12.0051, 12.0052, 12.0057
- Vindesine 12.0002, 12.0053

Hematologic Malignancies: general
- Cyclophosphamide 15.0035
- Hydroxyurea 5.0021
- Nitrogen Mustard 15.0035
- Vitamin C 15.0035

Histiocytosis
- Cyclophosphamide 5.0018
- 6-Mercaptopurine 5.0018
- Methotrexate 5.0018
- Prednisone 5.0018
- Radiation: Low-LET Co-60 gamma rays 5.0018, 17.0074
- Radiation: Low-LET photons 1-4 MeV 5.0018, 17.0074
- Vinblastine 5.0018

Hodgkin's Disease *see* Lymphoma

Kidney *see* Genitourinary Tumors

Larynx *see* Head and Neck Tumors

Leukemia: Acute Leukemia (general)
- Acetaminophen 17.0086
- Adriamycin 6.0017, 6.0049, 6.0081, 6.0097
- Amphotericin-B 15.0020
- AMSA 6.0077, 6.0083, 6.0091, 6.0097, 15.0014, 15.0067
- Antibiotics 6.0093
- Asparaginase, L- 6.0012, 6.0017, 6.0093
- Azacytidine 6.0049, 6.0078
- BCG-Glaxo 6.0059
- BCG-Tice 15.0057
- BCNU 6.0093
- Benadryl 6.0080, 17.0086
- Bone Marrow Therapy: Autologous 6.0088, 6.0093
- Bone Marrow Transplant 6.0097, 6.0102
- Citrovorum Factor 6.0017, 6.0059, 6.0093
- Corynebacterium Parvum-unspecified 6.0049
- Cyclophosphamide 6.0012, 6.0017, 6.0093
- Cytosine Arabinoside 6.0012, 6.0017, 6.0049, 6.0059, 6.0081, 6.0093, 6.0097
- Daunomycin 6.0012, 6.0049, 6.0059
- Dianhydrogalactitol 15.0001
- Hydrocortisone 6.0012, 6.0017, 6.0083, 6.0093
- Immunotherapy: General 6.0008
- Levamisole 6.0081
- Lithium Carbonate 6.0089, 6.0100, 6.0105
- MER-BCG 6.0097, 6.0100
- 6-Mercaptopurine 6.0012, 6.0017, 6.0097
- Methotrexate 6.0012, 6.0017, 6.0059, 6.0093, 6.0097, 6.0102
- Neocarzinostatin 17.0086, 17.0164

Nonspecific Stimulants 6.0049, 6.0059, 6.0081, 6.0097, 6.0100, 15.0057
Piperazinedione 6.0088, 6.0102, 15.0064
Platelets 6.0084, 6.0085
Prednimustine 6.0076
Prednisone 6.0012, 6.0017, 6.0081, 6.0093, 6.0097
Radiation: Low-LET Co-60 gamma rays 6.0012
Radiation: Low-LET photons 1-4 MeV 6.0012
Radiation: Low-LET photons above 4 MeV 6.0012, 6.0088
Radiation: Low-LET, unspecified 6.0102
Rubidazone 6.0080, 6.0081, 6.0093
Thioguanine 6.0017, 6.0049, 6.0093
Trimethoprim 6.0105, 15.0020
Tumor Cells/Cell Fractions 6.0049, 6.0059
Vincristine 6.0012, 6.0017, 6.0081, 6.0093, 6.0097
Vindesine 6.0094
VM-26 17.0175
VP-16 6.0093, 17.0175

Leukemia: Acute Lymphocytic Leukemia
Acetaminophen 17.0086
Actinomycin-D 6.0019, 6.0024, 6.0029, 15.0043
Adriamycin 6.0003, 6.0004, 6.0010, 6.0015, 6.0016, 6.0019, 6.0020, 6.0022, 6.0024, 6.0025, 6.0026, 6.0027, 6.0029, 6.0030, 6.0079, 15.0043, 15.0063
Anguidine 6.0014
Antibiotics 6.0093
Antibody Therapy 6.0104
Asparaginase, L- 6.0002, 6.0003, 6.0004, 6.0005, 6.0007, 6.0009, 6.0011, 6.0012, 6.0016, 6.0019, 6.0020, 6.0021, 6.0022, 6.0024, 6.0026, 6.0027, 6.0029, 6.0030, 6.0093, 15.0031, 15.0043, 15.0065, 17.0076, 17.0077, 17.0079
AZQ 6.0087
Bacteria/Bacterial Substances 15.0043
BCNU 6.0019, 6.0024, 6.0029, 6.0093, 6.0101, 15.0043
Benadryl 17.0086
Bleomycin 6.0022
Bone Marrow Therapy: Autologous 6.0093, 6.0101
Bone Marrow Transplant 6.0058, 6.0102, 6.0103
Chlorambucil 6.0104
Citrovorum Factor 6.0004, 6.0007, 6.0013, 6.0015, 6.0020, 6.0025, 6.0027, 6.0030, 6.0093, 15.0063, 17.0077
Corynebacterium Parvum-Burroughs 6.0107
Corynebacterium Parvum-unspecified 6.0022
Cyclophosphamide 6.0003, 6.0004, 6.0007, 6.0010, 6.0012, 6.0015, 6.0016, 6.0019, 6.0022, 6.0024, 6.0025, 6.0026, 6.0027, 6.0029, 6.0030, 6.0079, 6.0093, 6.0101, 6.0103, 15.0043, 15.0063
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DTIC 8.0006, 8.0007, 8.0014, 17.0117
Gallium Nitrate 8.0049, 15.0013
Hexamethylmelamine 11.0019, 17.0120, 17.0168
Interferon 15.0037
Levamisole 8.0010
Maytansine 17.0121
MER-BCG 8.0004
Methyl-GAG 8.0055
Nitrogen Mustard 8.0001, 8.0006, 8.0009, 8.0010, 8.0012, 8.0013, 8.0015, 8.0016, 8.0017, 17.0116, 17.0117
Nonspecific Stimulants 8.0004, 8.0010
PALA 8.0048
cis-Platinum 17.0120
Prednisolone 8.0017
Prednisone 8.0001, 8.0002, 8.0003, 8.0004, 8.0005, 8.0006, 8.0007, 8.0008, 8.0009, 8.0010, 8.0011, 8.0012, 8.0013, 8.0014, 8.0015, 8.0016, 8.0017, 8.0051, 17.0116, 17.0117, 17.0120
Procarbazine 8.0001, 8.0002, 8.0003, 8.0004, 8.0005, 8.0006, 8.0007, 8.0008, 8.0009, 8.0010, 8.0012, 8.0013, 8.0015, 8.0016, 8.0017, 17.0116, 17.0117
Radiation: Low-LET Co-60 gamma rays 8.0001, 8.0002, 8.0003, 8.0005, 8.0008, 8.0009, 8.0010, 8.0015, 8.0047, 17.0116, 17.0117
Radiation: Low-LET photons 1-4 MeV 8.0001, 8.0002, 8.0003, 8.0005, 8.0006, 8.0008, 8.0009, 8.0010, 8.0013, 8.0047, 17.0116, 17.0117

Radiation: Low-LET photons above 4 MeV 8.0002, 8.0003, 8.0005, 8.0006, 8.0009, 8.0010, 8.0047, 17.0116
Radiation: Low-LET, unspecified 8.0016, 8.0017
Streptozotocin 8.0004, 8.0005, 8.0012, 15.0026
Vinblastine 8.0003, 8.0004, 8.0005, 8.0006, 8.0007, 8.0008, 11.0021, 17.0117
Vincristine 8.0001, 8.0002, 8.0004, 8.0005, 8.0006, 8.0009, 8.0010, 8.0011, 8.0012, 8.0013, 8.0016, 8.0017, 17.0116, 17.0117, 17.0120
Vindesine 8.0051
Vitamin B 17.0120
VM-26 8.0055, 17.0120

Lymphoma: Lymphosarcoma
Actinomycin-D 15.0043
Adriamycin 6.0010, 8.0054, 15.0043
Asparaginase, L- 15.0043
Bacteria/Bacterial Substances 15.0043
BCNU 15.0043
Bleomycin 8.0054
Chlorozotocin 15.0003
Cyclophosphamide 6.0010, 15.0043, 17.0122
Cytosine Arabinoside 6.0010, 8.0054, 15.0043
Isophosphamide 8.0054
6-Mercaptopurine 6.0010, 15.0043
Methotrexate 6.0010, 8.0054, 15.0043
Methylprednisolone 6.0010
Nitrogen Mustard 17.0122
Prednisone 6.0010, 8.0054, 15.0043, 17.0122
Procarbazine 17.0122
Radiation: Low-LET Co-60 gamma rays 6.0010
Radiation: Low-LET photons 1-4 MeV 6.0010
Radiation: Low-LET photons above 4 MeV 6.0010
Radiation: Low-LET, unspecified 15.0043, 17.0122
Surgery 17.0122
Thioguanine 15.0043
Vincristine 6.0010, 8.0054, 15.0043, 17.0122
VP-16 8.0054

Lymphoma: Reticulum Cell Sarcoma
Actinomycin-D 15.0043
Adriamycin 8.0031, 8.0041, 15.0043
AMSA 8.0047, 8.0050
Antibiotics 8.0031
Asparaginase, L- 15.0043
Bacteria/Bacterial Substances 15.0043
BCG-Unspecified 8.0042
BCNU 15.0043
Bleomycin 8.0031, 8.0041
Citrovorum Factor 8.0020
Cyclophosphamide 8.0031, 8.0041, 8.0042, 15.0043, 17.0122
Cytosine Arabinoside 8.0031, 15.0043
Dexamethasone 8.0020, 8.0042
6-Mercaptopurine 15.0043
Methotrexate 8.0020, 15.0043
Nitrogen Mustard 17.0122
Nonspecific Stimulants 8.0042
Prednisone 8.0031, 8.0041, 8.0042, 15.0043, 17.0122
Procarbazine 8.0020, 8.0041, 8.0042, 17.0122
Radiation: Low-LET Co-60 gamma rays 8.0042, 8.0047
Radiation: Low-LET photons 1-4 MeV 8.0042, 8.0047
Radiation: Low-LET photons above 4 MeV 8.0042, 8.0047
Radiation: Low-LET, unspecified 15.0043, 17.0122
Surgery 17.0122
Thioguanine 15.0043
Vincristine 8.0031, 8.0041, 8.0042, 15.0043, 17.0122
VM-26 8.0020

Lymphoma: other
Adriamycin 8.0019, 8.0028, 8.0036, 8.0037, 8.0038, 8.0045, 8.0046, 8.0054, 8.0056, 15.0063, 15.0074
AMSA 8.0048
Antibody Therapy 15.0047
Asparaginase, L- 15.0065
Bleomycin 8.0019, 8.0028, 8.0036, 8.0054, 15.0062, 15.0074
Bone Marrow Therapy: Autologous 8.0057
Carminomycin 8.0045, 8.0046
CCNU 8.0028
Chlorambucil 15.0074
Citrovorum Factor 8.0019, 8.0037, 8.0038, 8.0056, 15.0063
Cyclophosphamide 8.0019, 8.0028, 8.0036, 8.0037, 8.0038, 8.0039, 8.0046, 8.0056, 8.0057, 15.0063, 15.0074
Cytosine Arabinoside 8.0037, 8.0039, 8.0054, 8.0057, 15.0063, 15.0065
Interferon 15.0054
Isophosphamide 8.0054
6-Mercaptopurine 8.0039, 15.0065
Methotrexate 8.0019, 8.0036, 8.0037, 8.0038, 8.0039, 8.0054, 8.0056, 15.0063, 15.0065
Methyl-GAG 8.0055
Nitrogen Mustard 8.0038, 8.0056
Nonspecific Stimulants 15.0054
PALA 8.0048
Poly IC 15.0054
Prednisone 8.0019, 8.0028, 8.0036, 8.0037, 8.0038, 8.0039, 8.0046, 8.0054, 8.0056, 15.0065, 15.0074
Procarbazine 8.0038, 8.0056
Radiation: Low-LET Co-60 gamma rays 8.0039, 8.0044, 15.0065
Radiation: Low-LET photons 1-4 MeV 8.0039, 15.0063, 15.0065
Radiation: Low-LET photons above 4 MeV 8.0039
Radiation: Low-LET, unspecified 8.0038, 8.0045, 8.0056, 8.0057, 15.0074
Surgery 8.0037, 8.0056, 15.0074
Vincristine 8.0019, 8.0028, 8.0036, 8.0037, 8.0038, 8.0039, 8.0046, 8.0054, 8.0056, 15.0063, 15.0065, 15.0074

VM-26 8.0055, 15.0062, 15.0065
VP-16 8.0038, 8.0045, 8.0046, 8.0054, 8.0056

Lymphoma: general
Adriamycin 6.0003, 6.0004, 6.0017, 6.0022, 8.0021, 8.0023, 8.0024, 8.0025, 8.0026, 8.0027, 8.0029, 8.0030, 8.0033, 8.0034, 8.0035, 8.0041, 8.0043, 8.0051, 17.0118, 17.0119
AMSA 8.0032, 8.0047, 8.0050, 15.0014, 15.0044, 15.0067, 15.0072
Asparaginase, L- 6.0003, 6.0004, 6.0017, 6.0022, 8.0018, 15.0031
Bacteria/Bacterial Substances 8.0035
BCG-Tice 15.0057
BCG-Unspecified 8.0026, 8.0029, 8.0034, 8.0042
BCNU 8.0018, 8.0024, 8.0051
Bleomycin 6.0022, 8.0021, 8.0023, 8.0029, 8.0030, 8.0033, 8.0034, 8.0041, 11.0021, 17.0118, 17.0119
CCNU 17.0118
Chlorambucil 8.0035, 17.0119
Chlorozotocin 15.0003, 15.0049
Citrovorum Factor 6.0004, 6.0017, 8.0020, 8.0027, 15.0029, 17.0118
Corynebacterium Parvum-unspecified 6.0022
Cyclophosphamide 6.0003, 6.0004, 6.0017, 6.0022, 8.0018, 8.0021, 8.0022, 8.0023, 8.0024, 8.0025, 8.0026, 8.0027, 8.0029, 8.0030, 8.0033, 8.0034, 8.0035, 8.0040, 8.0041, 8.0042, 8.0043, 17.0118, 17.0119
Cytosine Arabinoside 6.0003, 6.0004, 6.0017, 6.0022, 8.0018, 8.0026, 8.0030, 15.0029, 15.0032, 17.0118, 17.0119
Daunomycin 8.0018
Dexamethasone 8.0020, 8.0042, 15.0045
Dihydroxyanthracenedione 8.0052
Gallium Nitrate 8.0049, 15.0013
Hexamethylmelamine 11.0019, 17.0120, 17.0168
Hydrocortisone 6.0017, 8.0027, 15.0029
Hydroxyurea 8.0018
ICRF-159 15.0032
Immunotherapy: General 8.0033
Interferon 15.0037
Isophosphamide 8.0030, 15.0031
Levamisole 8.0026
Maytansine 17.0121
Melphalan 8.0035
6-Mercaptopurine 6.0003, 6.0004, 6.0017, 6.0022, 8.0027, 8.0043, 17.0118
Methotrexate 6.0003, 6.0004, 6.0017, 6.0022, 8.0018, 8.0020, 8.0027, 8.0030, 8.0043, 15.0029, 15.0031, 15.0045, 17.0118
Methyl-GAG 17.0169
Neocarzinostatin 17.0170
Nitrogen Mustard 8.0030, 17.0119
Nonspecific Stimulants 6.0022, 8.0026, 8.0029, 8.0034, 8.0042, 15.0057
cis-Platinum 5.0022, 17.0120
Prednisone 6.0003, 6.0004, 6.0017, 6.0022, 8.0018, 8.0021, 8.0022, 8.0023, 8.0024, 8.0025, 8.0027, 8.0029, 8.0030, 8.0033, 8.0034, 8.0035, 8.0040, 8.0041, 8.0042, 8.0043, 8.0051, 17.0118, 17.0119, 17.0120
Procarbazine 8.0020, 8.0023, 8.0030, 8.0041, 8.0042, 17.0119
Radiation: Low-LET Co-60 gamma rays 6.0003, 6.0004, 8.0018, 8.0022, 8.0023, 8.0025, 8.0027, 8.0029, 8.0034, 8.0042, 8.0047, 17.0118
Radiation: Low-LET photons 1-4 MeV 6.0003, 6.0004, 8.0018, 8.0022, 8.0023, 8.0027, 8.0033, 8.0034, 8.0042, 8.0047, 15.0045, 17.0118
Radiation: Low-LET photons above 4 MeV 6.0003, 6.0004, 8.0022, 8.0023, 8.0027, 8.0033, 8.0034, 8.0042, 8.0047, 15.0029, 15.0045, 17.0118
Radiation: Low-LET, unspecified 8.0035, 17.0119
Spirogermanium 8.0053
Streptozotocin 15.0026
Surgery 8.0043
Thio-TEPA 8.0035, 15.0045
Thioguanine 6.0017, 8.0018, 17.0119
Vinblastine 11.0021, 17.0118
Vincristine 6.0003, 6.0004, 6.0017, 6.0022, 8.0018, 8.0021, 8.0023, 8.0024, 8.0025, 8.0026, 8.0027, 8.0029, 8.0030, 8.0033, 8.0034, 8.0035, 8.0040, 8.0041, 8.0042, 8.0043, 17.0118, 17.0119, 17.0120
Vindesine 8.0051
Virus/Viral Substances 8.0029, 8.0034
Vitamin B 17.0120
VM-26 8.0020, 17.0120
VP-16 8.0030

Lymphosarcoma *see* Lymphoma

Melanoma *see* Skin Tumors

Mesothelioma
Adriamycin 10.0020, 10.0032
AMSA 10.0013
Azacytidine 10.0020
Bleomycin 10.0031
Bruceantin 10.0031
Chlorozotocin 10.0031
Dibromodulcitol 10.0032
ICRF-159 10.0032
Maytansine 10.0032
Methyl-GAG 10.0031
Radiation: Low-LET, unspecified 10.0020

Mycosis Fungoides
Adriamycin 5.0020, 8.0026
Antibody Therapy 15.0047
BCG-Unspecified 8.0026
Bleomycin 5.0020
Cyclophosphamide 5.0020, 8.0026
Cytosine Arabinoside 8.0026
Levamisole 8.0026
Methyl-GAG 8.0055
Nonspecific Stimulants 8.0026

- Prednisone 5.0020
- Radiation: Low-LET electrons 5.0020
- Vincristine 5.0020, 8.0026
- VM-26 8.0055

Myeloma
- Adriamycin 5.0001, 5.0007, 5.0009, 5.0010, 5.0011, 5.0017
- AMSA 5.0003, 15.0016
- Azathioprine 5.0007
- BCNU 5.0001, 5.0004, 5.0007, 5.0009, 5.0010, 5.0011, 5.0014
- Bleomycin 5.0009
- CCNU 5.0017
- Chlorozotocin 5.0008, 17.0072
- Cyclophosphamide 5.0001, 5.0004, 5.0005, 5.0007, 5.0010, 5.0011, 5.0014, 5.0017
- Hexamethylmelamine 5.0005
- Interferon 5.0016, 15.0037, 15.0054
- Levamisole 5.0010
- Melphalan 5.0001, 5.0002, 5.0004, 5.0007, 5.0009, 5.0010, 5.0012, 5.0014, 5.0017
- Methyl-GAG 17.0169
- Nonspecific Stimulants 5.0010, 15.0054, 17.0073
- cis-Platinum 5.0009, 5.0022
- Poly IC 15.0054, 17.0073
- Prednisone 5.0001, 5.0002, 5.0004, 5.0006, 5.0007, 5.0008, 5.0009, 5.0010, 5.0011, 5.0012, 5.0014, 5.0017
- Radiation: Low-LET electrons 5.0002
- Radiation: Low-LET photons 1-4 MeV 5.0006
- Radiation: Low-LET photons above 4 MeV 5.0002, 5.0006, 5.0015
- Vinblastine 5.0011
- Vincristine 5.0004, 5.0007, 5.0009, 5.0010, 5.0011, 5.0014, 5.0017
- Vindesine 5.0013

Pediatric Solid Tumors: Ewing's Sarcoma
- Actinomycin-D 11.0012, 11.0013, 11.0014, 11.0016, 11.0017, 11.0018, 17.0149
- Adriamycin 10.0018, 10.0033, 11.0012, 11.0013, 11.0014, 11.0015, 11.0016, 11.0017, 11.0018, 17.0143, 17.0149
- Azacytidine 17.0138
- BCNU 11.0017
- Bone Marrow Therapy: Autologous 11.0015
- Corynebacterium Parvum-Burroughs 17.0143
- Cyclophosphamide 10.0018, 10.0033, 11.0012, 11.0013, 11.0014, 11.0015, 11.0016, 11.0017, 11.0018, 17.0143, 17.0149
- DTIC 10.0018, 10.0033, 11.0015, 11.0016
- 5-Fluorouracil 11.0013
- Methotrexate 11.0018, 17.0143
- Nonspecific Stimulants 17.0143
- Radiation: Low-LET Co-60 gamma rays 11.0012, 11.0013, 17.0149
- Radiation: Low-LET photons 1-4 MeV 11.0012, 11.0013, 11.0017, 17.0149
- Radiation: Low-LET photons above 4 MeV 11.0012, 17.0149
- Radiation: Low-LET, unspecified 11.0014, 11.0015, 11.0016, 11.0018
- Surgery 11.0012, 11.0013, 11.0015, 11.0018
- Vincristine 10.0018, 11.0012, 11.0013, 11.0014, 11.0015, 11.0016, 11.0017, 11.0018, 17.0149

Neuroblastoma *see* Pediatric Solid Tumors

Oat Cell Carcinoma *see* Lung Tumors

Ovary *see* Gynecologic Tumors

Pancreas *see* Gastrointestinal Tumors and Endocrine Tumors

Pediatric Solid Tumors: Neuroblastoma
- Adriamycin 11.0002, 11.0004, 11.0005, 11.0006, 11.0007, 11.0008, 11.0009, 17.0146
- BCG-Glaxo 11.0008
- Bleomycin 11.0021
- CCNU 13.0003, 17.0159
- Cyclophosphamide 11.0002, 11.0004, 11.0005, 11.0006, 11.0007, 11.0008, 11.0009, 17.0146
- DTIC 11.0002, 11.0004, 17.0146
- MER-BCG 11.0005
- Nitrogen Mustard 13.0017
- Nonspecific Stimulants 11.0005, 11.0008
- Nutritional Support 11.0024
- cis-Platinum 11.0002, 11.0003, 11.0006, 11.0007, 11.0009, 17.0150
- Prednisone 13.0003, 13.0017, 17.0159
- Procarbazine 13.0003, 13.0017, 17.0159
- Radiation: Low-LET Co-60 gamma rays 11.0004, 11.0005, 11.0008, 13.0003, 13.0017, 17.0159
- Radiation: Low-LET photons 1-4 MeV 11.0004, 11.0005, 11.0008, 13.0003, 13.0017, 17.0159
- Radiation: Low-LET photons above 4 MeV 11.0004, 11.0005, 11.0008, 13.0017
- Surgery 11.0004, 11.0008, 11.0009, 13.0017
- Tumor Cells/Cell Fractions 11.0008
- Vinblastine 11.0021
- Vincristine 11.0002, 11.0004, 11.0005, 11.0006, 11.0007, 13.0003, 13.0017, 17.0146, 17.0159
- VM-26 11.0002, 11.0003, 11.0008, 11.0009, 17.0146, 17.0175
- VP-16 17.0175

Pediatric Solid Tumors: Retinoblastoma
- Adriamycin 17.0152
- Cyclophosphamide 17.0151, 17.0152
- Methotrexate 17.0152
- Radiation: Low-LET Co-60 gamma rays 17.0152
- Radiation: Low-LET photons 1-4 MeV 17.0152
- Radiation: Low-LET photons above 4 MeV 17.0152
- Vincristine 17.0151, 17.0152

Pediatric Solid Tumors: Rhabdomyosarcoma
- Actinomycin-D 11.0010, 11.0011, 17.0148
- Adriamycin 10.0014, 10.0018, 10.0025, 10.0033, 11.0010, 11.0011, 17.0143, 17.0148

Azapicyl 17.0147
Bleomycin 10.0031
Bone Marrow Therapy: Autologous 11.0010
Bruceantin 10.0031
Chlorozotocin 10.0031
Citrovorum Factor 17.0148
Corynebacterium Parvum-Burroughs 17.0143
Cyclophosphamide 10.0018, 10.0033, 11.0010, 11.0011, 17.0143, 17.0148
Cytosine Arabinoside 17.0148
DTIC 10.0018, 10.0033
Methotrexate 17.0143, 17.0148
Methyl-GAG 10.0031
Nonspecific Stimulants 17.0143
Nutritional Support 11.0024
Radiation: Low-LET Co-60 gamma rays 11.0011, 17.0148
Radiation: Low-LET photons 1-4 MeV 11.0011, 17.0148
Radiation: Low-LET photons above 4 MeV 11.0011, 17.0148
Radiation: Low-LET, unspecified 10.0025, 11.0010
Surgery 10.0025, 11.0010, 11.0011, 17.0148
Vincristine 10.0018, 11.0010, 11.0011, 17.0148

Pediatric Solid Tumors: Wilms' Embryoma
Actinomycin-D 11.0001, 17.0145
Adriamycin 11.0001
Bleomycin 11.0021
Radiation: Low-LET Co-60 gamma rays 17.0145
Radiation: Low-LET photons 1-4 MeV 17.0145
Radiation: Low-LET, unspecified 11.0001
Surgery 11.0001
Vinblastine 11.0021
Vincristine 11.0001, 17.0145

Pediatric Solid Tumors: general
Actinomycin-D 11.0020, 15.0061
Adriamycin 11.0020
AMSA 11.0023
Benadryl 15.0061
Bleomycin 15.0061
CCNU 13.0004
Cyclophosphamide 11.0020, 15.0061
Dianhydrogalactitol 15.0001
Dihydroxyanthracenedione 15.0018
5-Fluorouracil 11.0020
Isophosphamide 11.0025
Lithium Carbonate 11.0020
Nitrogen Mustard 13.0013
Nonspecific Stimulants 11.0026
Piperazinedione 15.0064
cis-Platinum 15.0061, 17.0150
Poly IC 11.0026
Prednisone 13.0004, 13.0013
Procarbazine 13.0004, 13.0013
Radiation: Low-LET Co-60 gamma rays 13.0004
Radiation: Low-LET photons 1-4 MeV 13.0004
Radiation: Low-LET, unspecified 15.0061
Rubidazone 11.0022
Vinblastine 15.0061
Vincristine 11.0020, 13.0004, 13.0013, 15.0061
VM-26 17.0175
VP-16 17.0175

Pharynx *see* Head and Neck Tumors

Polycythemia Vera
Cimetidine 17.0075
Cytosine Arabinoside 6.0069
Hydroxyurea 5.0019, 5.0021
Prednisone 6.0069
Rubidazone 6.0069
Vincristine 6.0069

Prostate *see* Genitourinary Tumors

Rectum *see* Gastrointestinal Tumors

Reticulum Cell Sarcoma *see* Lymphoma

Retinoblastoma *see* Pediatric Solid Tumors

Rhabdomyosarcoma *see* Pediatric Solid Tumors

Sarcoma: Osteogenic Sarcoma
Actinomycin-D 10.0037, 15.0040
Adriamycin 10.0001, 10.0003, 10.0004, 10.0005, 10.0007, 10.0008, 10.0009, 10.0012, 10.0032, 10.0033, 10.0037, 10.0043, 11.0027, 15.0040, 17.0136, 17.0140, 17.0143
AMSA 10.0038
Azacytidine 17.0138
Bacteria/Bacterial Substances 10.0043
BCG-Tice 10.0043, 15.0057
BCG-Unspecified 15.0040
Bleomycin 10.0031, 10.0037, 11.0021
Bruceantin 10.0031
Chlorozotocin 10.0031, 10.0035
Citrovorum Factor 10.0001, 10.0003, 10.0004, 10.0006, 10.0007, 10.0009, 10.0012, 11.0027, 17.0136, 17.0140
Corynebacterium Parvum-Burroughs 17.0143
Cyclophosphamide 10.0003, 10.0004, 10.0005, 10.0007, 10.0009, 10.0033, 10.0037, 11.0027, 15.0040, 17.0136, 17.0143
Dibromodulcitol 10.0032
Dihydroxyanthracenedione 10.0036, 10.0041
DTIC 10.0007, 10.0033, 10.0037, 15.0040
Gallium Nitrate 17.0144
Hyperthermia 17.0166, 17.0167
ICRF-159 10.0032
Maytansine 10.0032
Melphalan 10.0003, 10.0005, 10.0007
Methotrexate 10.0001, 10.0003, 10.0004, 10.0006, 10.0007, 10.0009, 10.0010, 10.0012, 10.0043, 11.0027, 17.0136, 17.0140, 17.0143
Methyl-GAG 10.0031
Misonidazole 10.0042, 15.0009
Nonspecific Stimulants 10.0043, 15.0040, 15.0057, 17.0143

- PALA 10.0040
- cis-Platinum 10.0007, 10.0008, 10.0011, 10.0037, 17.0139, 17.0150
- Radiation: High-LET heavy ions 15.0005
- Radiation: Low-LET Co-60 gamma rays 10.0001, 10.0006, 10.0009, 10.0042, 15.0009, 17.0167
- Radiation: Low-LET photons 1-4 MeV 10.0001, 10.0006, 10.0009, 10.0042, 15.0009, 17.0167
- Radiation: Low-LET photons above 4 MeV 10.0006, 10.0009, 10.0042, 15.0009, 17.0167
- Radiation: Low-LET, unspecified 17.0166
- Surgery 10.0004, 10.0007, 10.0008, 11.0027
- Tumor Cells/Cell Fractions 10.0043
- Vinblastine 10.0039, 11.0021
- Vincristine 10.0001, 10.0003, 10.0004, 10.0005, 10.0006, 10.0007, 10.0009, 10.0012, 10.0037, 15.0040
- Vindesine 10.0039
- Virus/Viral Substances 15.0040

Sarcoma: Soft Tissue Sarcoma

- Actinomycin-D 10.0026, 10.0034, 10.0037, 15.0040, 17.0148
- Adriamycin 4.0060, 10.0014, 10.0015, 10.0016, 10.0018, 10.0019, 10.0020, 10.0021, 10.0022, 10.0023, 10.0024, 10.0025, 10.0026, 10.0027, 10.0028, 10.0030, 10.0032, 10.0033, 10.0034, 10.0037, 10.0043, 15.0040, 17.0141, 17.0143, 17.0148
- Amphotericin-B 10.0034
- AMSA 10.0013, 10.0038
- Azacytidine 10.0020
- Azapicyl 17.0147
- Bacteria/Bacterial Substances 10.0019, 10.0043
- BCG-Tice 10.0043, 15.0057
- BCG-Unspecified 15.0040
- Bleomycin 10.0031, 10.0037, 11.0021
- Bruceantin 10.0031
- Carminomycin 10.0030
- Chlorozotocin 10.0031, 10.0035
- Citrovorum Factor 10.0021, 10.0022, 10.0023, 10.0024, 15.0071, 17.0148
- Corynebacterium Parvum-Burroughs 17.0143
- Cyclophosphamide 10.0016, 10.0018, 10.0019, 10.0021, 10.0022, 10.0023, 10.0024, 10.0026, 10.0027, 10.0028, 10.0033, 10.0034, 10.0037, 15.0040, 17.0143, 17.0148
- Cytosine Arabinoside 17.0148
- DDMP 15.0071
- Dibromodulcitol 10.0032
- Diglycoaldehyde 17.0165
- Dihydroxyanthracenedione 10.0017, 10.0036, 10.0041
- DTIC 10.0015, 10.0018, 10.0026, 10.0027, 10.0028, 10.0033, 10.0037, 15.0040, 17.0141
- Gallium Nitrate 17.0144
- Hyperthermia 10.0016, 17.0166, 17.0167
- ICRF-159 10.0032
- Maytansine 10.0032
- Methotrexate 10.0021, 10.0022, 10.0023, 10.0024, 10.0034, 10.0043, 17.0142, 17.0143, 17.0148
- Methyl-GAG 10.0031
- Misonidazole 10.0024, 15.0009
- Nonspecific Stimulants 10.0043, 15.0040, 15.0057, 17.0143
- PALA 10.0029, 10.0040
- cis-Platinum 10.0026, 10.0037, 15.0021
- Radiation: High-LET heavy ions 15.0005
- Radiation: Low-LET Co-60 gamma rays 15.0009, 17.0141, 17.0148, 17.0167
- Radiation: Low-LET electrons 10.0024, 17.0141
- Radiation: Low-LET photons 1-4 MeV 15.0009, 17.0148, 17.0167
- Radiation: Low-LET photons above 4 MeV 15.0009, 17.0148, 17.0167
- Radiation: Low-LET, unspecified 10.0020, 10.0021, 10.0022, 10.0023, 10.0024, 10.0025, 17.0166
- Surgery 10.0021, 10.0022, 10.0024, 10.0025, 17.0148
- Tumor Cells/Cell Fractions 10.0043
- Vinblastine 10.0039, 11.0021
- Vincristine 10.0018, 10.0019, 10.0026, 10.0027, 10.0028, 10.0037, 15.0040, 17.0148
- Vindesine 10.0039
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Sarcoma: Osteogenic Sarcoma 15.0005
Sarcoma: Soft Tissue Sarcoma 15.0005
Skin Tumors: Melanoma 9.0002
Solid Tumors: general 15.0005

Radiation: High-LET neutrons
Brain and other CNS Tumors 13.0009, 13.0012
Gastrointestinal Tumors: Esophagus 2.0004
Gastrointestinal Tumors: Pancreas 2.0044
Genitourinary Tumors: Bladder 3.0004
Genitourinary Tumors: Prostate 3.0053
Gynecologic Tumors: Cervix 4.0009, 4.0015
Head and Neck Tumors 12.0008, 12.0057
Lung Tumors: Non-Oat Cell 7.0042, 7.0044
Skin Tumors: Melanoma 9.0003

Radiation: High-LET pions
Gastrointestinal Tumors: Colon and Rectum 2.0073
Genitourinary Tumors: Bladder 3.0006
Head and Neck Tumors 12.0012
Solid Tumors: general 14.0001, 14.0002

Radiation: Low-LET Co-60 gamma rays
Body Sites/Tumor Types: general 15.0008, 15.0011
Body Sites: Multiple 10.0002, 17.0167
Brain and other CNS Tumors 13.0002, 13.0003, 13.0004, 13.0005, 13.0006, 13.0007, 13.0008, 13.0010, 13.0011, 13.0014, 13.0015, 13.0017, 13.0019, 13.0027, 13.0033, 13.0039, 13.0041, 17.0159, 17.0160, 17.0161
Breast Cancer 1.0001, 1.0021, 1.0027, 1.0028, 1.0030, 1.0040, 1.0066, 1.0089, 1.0092, 1.0093, 1.0099, 15.0011, 17.0167
Carcinoid 2.0051, 2.0052
Endocrine Tumors: Endocrine Pancreas 2.0046
Gastrointestinal Tumors: Colon and Rectum 2.0071, 2.0072, 2.0073, 2.0081, 2.0083, 2.0100, 2.0112, 2.0117, 2.0119, 15.0011, 17.0030, 17.0032, 17.0036, 17.0037, 17.0046, 17.0048, 17.0167
Gastrointestinal Tumors: Esophagus 2.0004, 2.0005, 2.0015, 2.0016, 17.0167
Gastrointestinal Tumors: Liver 2.0054, 2.0055, 2.0056, 2.0057, 2.0129, 17.0048
Gastrointestinal Tumors: Pancreas 2.0046, 2.0051, 2.0052, 2.0129, 17.0048, 17.0167
Gastrointestinal Tumors: Stomach 2.0129, 17.0048
Gastrointestinal Tumors: general 15.0010
Genitourinary Tumors: Bladder 3.0004, 3.0005, 3.0006, 3.0021, 15.0006, 17.0054, 17.0167

Genitourinary Tumors: Kidney 17.0145
Genitourinary Tumors: Prostate 3.0052, 3.0053, 3.0054, 3.0064
Gynecologic Tumors: Cervix 4.0002, 4.0009, 4.0010, 4.0011, 4.0012, 4.0022, 4.0023, 15.0006, 15.0010
Gynecologic Tumors: Ovary 2.0051, 4.0025, 4.0046, 4.0048, 4.0053, 15.0002, 15.0010
Gynecologic Tumors: Uterus 4.0061, 4.0064, 15.0010
Gynecologic Tumors: Vagina 4.0080
Gynecologic Tumors: Vulva 4.0080
Head and Neck Tumors 8.0039, 12.0006, 12.0008, 12.0009, 12.0010, 12.0011, 12.0012, 12.0013, 12.0014, 12.0015, 12.0017, 12.0021, 12.0022, 12.0023, 12.0027, 12.0030, 12.0037, 12.0042, 12.0046, 12.0048, 12.0049, 12.0051, 12.0056, 12.0057, 12.0058, 15.0006, 17.0158, 17.0167
Histiocytosis 5.0018, 17.0074
Leukemia: Acute Leukemia (general) 6.0012
Leukemia: Acute Lymphocytic Leukemia 6.0002, 6.0003, 6.0004, 6.0005, 6.0007, 6.0010, 6.0012, 6.0013, 6.0016, 6.0018, 6.0027, 15.0065, 17.0076, 17.0079
Leukemia: Acute Nonlymphocytic Leukemia 6.0006, 6.0032
Leukemia: Chronic Lymphocytic Leukemia 17.0085
Leukemia: Extramedullary Leukemia 6.0018, 17.0076
Leukemia: general 8.0027
Lung Tumors: Oat Cell 7.0001, 7.0002, 7.0007, 7.0008, 7.0010, 7.0011, 7.0013, 7.0019, 7.0020, 7.0021, 7.0029, 7.0034, 7.0098, 17.0087, 17.0092
Lung Tumors: general 17.0167
Lung Tumors: Non-Oat Cell 7.0040, 7.0043, 7.0046, 7.0047, 7.0049, 7.0054, 7.0061, 7.0062, 7.0071, 7.0085, 7.0097, 7.0098, 17.0095, 17.0097, 17.0112
Lymphoma: Hodgkin's Disease 8.0001, 8.0002, 8.0003, 8.0005, 8.0008, 8.0009, 8.0010, 8.0015, 8.0047, 17.0116, 17.0117
Lymphoma: Lymphosarcoma 6.0010
Lymphoma: Reticulum Cell Sarcoma 8.0042, 8.0047
Lymphoma: other 8.0039, 8.0044, 15.0065
Lymphoma: general 6.0003, 6.0004, 8.0018, 8.0022, 8.0023, 8.0025, 8.0027, 8.0029, 8.0034, 8.0042, 8.0047, 17.0118
Pediatric Solid Tumors: Ewing's Sarcoma 11.0012, 11.0013, 17.0149
Pediatric Solid Tumors: Neuroblastoma 11.0004, 11.0005, 11.0008, 13.0003, 13.0017, 17.0159
Pediatric Solid Tumors: Retinoblastoma 17.0152
Pediatric Solid Tumors: Rhabdomyosarcoma 11.0011, 17.0148
Pediatric Solid Tumors: Wilms' Embryoma 17.0145
Pediatric Solid Tumors: general 13.0004
Sarcoma: Osteogenic Sarcoma 10.0001, 10.0006, 10.0009, 10.0042, 15.0009, 17.0167
Sarcoma: Soft Tissue Sarcoma 15.0009, 17.0141, 17.0148, 17.0167
Skin Tumors: Melanoma 9.0009, 15.0009, 17.0167
Skin Tumors: Non-melanoma 17.0167

Radiation: Low-LET electrons
  Body Sites: Multiple 15.0007
  Breast Cancer 1.0040, 1.0088, 1.0093
  Gastrointestinal Tumors: Stomach 2.0032
  Genitourinary Tumors: Bladder 3.0005
  Genitourinary Tumors: Testis 3.0068
  Head and Neck Tumors 12.0014, 12.0046
  Lung Tumors: Non-Oat Cell 17.0112
  Mycosis Fungoides 5.0020
  Myeloma 5.0002
  Sarcoma: Soft Tissue Sarcoma 10.0024, 17.0141
  Solid Tumors: general 15.0007

Radiation: Low-LET Implant
  Body Sites: Multiple 15.0007
  Breast Cancer 1.0040, 1.0071, 1.0093
  Gynecologic Tumors: Cervix 4.0002, 4.0010, 4.0012, 4.0015, 4.0021, 4.0022, 4.0023
  Gynecologic Tumors: Ovary 4.0029
  Gynecologic Tumors: Uterus 4.0064
  Gynecologic Tumors: Vagina 4.0069
  Gynecologic Tumors: Vulva 4.0069
  Head and Neck Tumors 12.0010, 12.0046
  Solid Tumors: general 15.0007

Radiation: Low-LET photons 1-4 MeV
  Body Sites/Tumor Types: general 15.0008, 15.0011
  Body Sites: Multiple 10.0002, 17.0167
  Brain and other CNS Tumors 13.0002, 13.0003, 13.0004, 13.0005, 13.0006, 13.0007, 13.0008, 13.0010, 13.0011, 13.0012, 13.0014, 13.0015, 13.0017, 13.0019, 13.0027, 17.0159, 17.0160, 17.0161
  Breast Cancer 1.0001, 1.0008, 1.0021, 1.0027, 1.0028, 1.0030, 1.0040, 1.0071, 1.0074, 1.0089, 1.0092, 1.0093, 1.0099, 1.0104, 15.0011, 15.0012, 15.0045, 17.0167
  Carcinoid 2.0051, 2.0052
  Endocrine Tumors: Endocrine Pancreas 2.0046
  Gastrointestinal Tumors: Colon and Rectum 2.0071, 2.0072, 2.0081, 2.0083, 2.0098, 2.0100, 2.0112, 2.0117, 2.0119, 15.0011, 17.0030, 17.0032, 17.0036, 17.0037, 17.0046, 17.0048, 17.0167
  Gastrointestinal Tumors: Esophagus 2.0004, 2.0005, 2.0006, 2.0015, 2.0016, 17.0167
  Gastrointestinal Tumors: Liver 2.0054, 2.0055, 2.0056, 2.0057, 2.0129, 17.0048
  Gastrointestinal Tumors: Pancreas 2.0046, 2.0047, 2.0051, 2.0052, 2.0129, 17.0048, 17.0167
  Gastrointestinal Tumors: Stomach 2.0129, 17.0048
  Gastrointestinal Tumors: general 15.0010
  Genitourinary Tumors: Bladder 3.0001, 3.0005, 3.0006, 3.0021, 15.0006, 17.0054, 17.0167
  Genitourinary Tumors: Kidney 17.0145
  Genitourinary Tumors: Prostate 3.0046, 3.0052, 3.0053, 3.0054, 3.0064, 15.0012
  Genitourinary Tumors: Testis 3.0068
  Gynecologic Tumors: Cervix 4.0002, 4.0010, 4.0011, 4.0012, 15.0006, 15.0010

Gynecologic Tumors: Ovary 2.0051, 4.0025, 4.0046, 4.0048, 4.0053, 15.0002, 15.0010

Gynecologic Tumors: Uterus 4.0061, 4.0064, 15.0010

Gynecologic Tumors: Vagina 4.0080

Gynecologic Tumors: Vulva 4.0080

Head and Neck Tumors 8.0039, 12.0009, 12.0010, 12.0012, 12.0013, 12.0014, 12.0015, 12.0017, 12.0021, 12.0022, 12.0023, 12.0027, 12.0030, 12.0037, 12.0046, 12.0048, 12.0049, 12.0051, 15.0006, 17.0158, 17.0167

Histiocytosis 5.0018, 17.0074

Leukemia: Acute Leukemia (general) 6.0012

Leukemia: Acute Lymphocytic Leukemia 6.0002, 6.0003, 6.0004, 6.0005, 6.0007, 6.0010, 6.0012, 6.0013, 6.0016, 6.0018, 15.0063, 15.0065, 17.0076, 17.0079

Leukemia: Acute Nonlymphocytic Leukemia 6.0006, 6.0032

Leukemia: Chronic Lymphocytic Leukemia 6.0063, 17.0085

Leukemia: Extramedullary Leukemia 6.0018, 17.0076

Leukemia: general 8.0027, 15.0045

Lung Tumors: Oat Cell 7.0001, 7.0002, 7.0007, 7.0008, 7.0010, 7.0011, 7.0013, 7.0014, 7.0019, 7.0020, 7.0021, 7.0033, 7.0034, 7.0098, 17.0087, 17.0092

Lung Tumors: general 15.0012, 17.0167

Lung Tumors: Non-Oat Cell 7.0040, 7.0043, 7.0044, 7.0045, 7.0046, 7.0047, 7.0049, 7.0054, 7.0061, 7.0062, 7.0065, 7.0071, 7.0097, 7.0098, 17.0095, 17.0097, 17.0112, 17.0113

Lymphoma: Hodgkin's Disease 8.0001, 8.0002, 8.0003, 8.0005, 8.0006, 8.0008, 8.0009, 8.0010, 8.0013, 8.0047, 17.0116, 17.0117

Lymphoma: Lymphosarcoma 6.0010

Lymphoma: Reticulum Cell Sarcoma 8.0042, 8.0047

Lymphoma: other 8.0039, 15.0063, 15.0065

Lymphoma: general 6.0003, 6.0004, 8.0018, 8.0022, 8.0023, 8.0027, 8.0033, 8.0034, 8.0042, 8.0047, 15.0045, 17.0118

Myeloma 5.0006

Pediatric Solid Tumors: Ewing's Sarcoma 11.0012, 11.0013, 11.0017, 17.0149

Pediatric Solid Tumors: Neuroblastoma 11.0004, 11.0005, 11.0008, 13.0003, 13.0017, 17.0159

Pediatric Solid Tumors: Retinoblastoma 17.0152

Pediatric Solid Tumors: Rhabdomyosarcoma 11.0011, 17.0148

Pediatric Solid Tumors: Wilms' Embryoma 17.0145

Pediatric Solid Tumors: general 13.0004

Sarcoma: Osteogenic Sarcoma 10.0001, 10.0006, 10.0009, 10.0042, 15.0009, 17.0167

Sarcoma: Soft Tissue Sarcoma 15.0009, 17.0148, 17.0167

Skin Tumors: Melanoma 9.0009, 15.0009, 15.0045, 17.0167

Skin Tumors: Non-melanoma 17.0167

Radiation: Low-LET photons above 4 MeV

Body Sites/Tumor Types: general 15.0008, 15.0011

Body Sites: Multiple 10.0002, 15.0007, 17.0167

Brain and other CNS Tumors 13.0002, 13.0005, 13.0006, 13.0007, 13.0008, 13.0010, 13.0011, 13.0012, 13.0014, 13.0015, 13.0017, 13.0019, 13.0027, 13.0033, 15.0029, 17.0160, 17.0161

Breast Cancer 1.0001, 1.0008, 1.0021, 1.0028, 1.0030, 1.0071, 1.0089, 1.0092, 1.0093, 1.0099, 15.0011, 15.0012, 15.0045, 17.0167

Carcinoid 2.0051, 2.0052

Endocrine Tumors: Endocrine Pancreas 2.0046

Gastrointestinal Tumors: Colon and Rectum 2.0071, 2.0072, 2.0073, 2.0081, 2.0083, 2.0100, 2.0117, 2.0119, 15.0011, 17.0030, 17.0032, 17.0036, 17.0037, 17.0046, 17.0167

Gastrointestinal Tumors: Esophagus 2.0005, 2.0006, 2.0015, 2.0016, 17.0167

Gastrointestinal Tumors: Liver 2.0054, 2.0055, 2.0056, 2.0129

Gastrointestinal Tumors: Pancreas 2.0046, 2.0047, 2.0051, 2.0052, 2.0129, 17.0167

Gastrointestinal Tumors: Stomach 2.0129

Gastrointestinal Tumors: general 15.0010

Genitourinary Tumors: Bladder 3.0001, 3.0003, 3.0004, 3.0005, 3.0006, 3.0021, 3.0025, 17.0054, 17.0167

Genitourinary Tumors: Prostate 3.0046, 3.0053, 3.0064, 15.0012

Gynecologic Tumors: Cervix 4.0002, 4.0009, 4.0010, 4.0011, 4.0012, 4.0015, 15.0010

Gynecologic Tumors: Ovary 2.0051, 4.0025, 4.0034, 4.0046, 4.0048, 4.0053, 15.0002, 15.0010

Gynecologic Tumors: Uterus 4.0061, 4.0064, 15.0010

Gynecologic Tumors: Vagina 4.0069, 4.0080

Gynecologic Tumors: Vulva 4.0069, 4.0080

Head and Neck Tumors 8.0039, 12.0006, 12.0008, 12.0009, 12.0010, 12.0011, 12.0012, 12.0013, 12.0014, 12.0015, 12.0017, 12.0023, 12.0027, 12.0030, 12.0037, 12.0046, 12.0048, 12.0049, 12.0051, 17.0158, 17.0167

Leukemia: Acute Leukemia (general) 6.0012, 6.0088

Leukemia: Acute Lymphocytic Leukemia 6.0002, 6.0003, 6.0004, 6.0005, 6.0007, 6.0010, 6.0012, 6.0013, 6.0016, 6.0018, 17.0076

Leukemia: Acute Nonlymphocytic Leukemia 6.0006, 6.0032

Leukemia: Chronic Lymphocytic Leukemia 17.0085

Leukemia: Chronic Nonlymphocytic Leukemia 6.0088

Leukemia: Extramedullary Leukemia 6.0018, 17.0076

Leukemia: general 8.0027, 15.0045

Lung Tumors: Oat Cell 7.0001, 7.0002, 7.0007, 7.0008, 7.0011, 7.0013, 7.0014, 7.0020, 7.0021, 7.0031, 7.0034, 17.0087, 17.0092, 17.0093

Lung Tumors: general 15.0012, 17.0167

Lung Tumors: Non-Oat Cell 7.0040, 7.0043, 7.0044, 7.0045, 7.0046, 7.0054, 7.0061, 7.0062, 7.0065, 7.0071, 17.0095, 17.0097

Lymphoma: Hodgkin's Disease 8.0002, 8.0003, 8.0005, 8.0006, 8.0009, 8.0010, 8.0047, 17.0116

Lymphoma: Lymphosarcoma 6.0010

Lymphoma: Reticulum Cell Sarcoma 8.0042, 8.0047

- Lymphoma: other 8.0039
- Lymphoma: general 6.0003, 6.0004, 8.0022, 8.0023, 8.0027, 8.0033, 8.0034, 8.0042, 8.0047, 15.0029, 15.0045, 17.0118
- Myeloma 5.0002, 5.0006, 5.0015
- Pediatric Solid Tumors: Ewing's Sarcoma 11.0012, 17.0149
- Pediatric Solid Tumors: Neuroblastoma 11.0004, 11.0005, 11.0008, 13.0017
- Pediatric Solid Tumors: Retinoblastoma 17.0152
- Pediatric Solid Tumors: Rhabdomyosarcoma 11.0011, 17.0148
- Sarcoma: Osteogenic Sarcoma 10.0006, 10.0009, 10.0042, 15.0009, 17.0167
- Sarcoma: Soft Tissue Sarcoma 15.0009, 17.0148, 17.0167
- Skin Tumors: Melanoma 9.0009, 15.0009, 15.0045, 17.0167
- Skin Tumors: Non-melanoma 17.0167
- Solid Tumors: general 15.0007, 15.0050

Radiation: Low-LET, unspecified
- Body Sites/Tumor Types: general 15.0052, 15.0056, 17.0137
- Brain and other CNS Tumors 1.0049, 7.0016, 9.0022, 13.0035, 13.0036, 13.0037, 13.0038, 13.0040, 14.0006, 14.0007
- Breast Cancer 1.0049, 1.0053, 1.0054, 1.0073, 14.0006, 14.0007, 17.0008, 17.0166
- Gastrointestinal Tumors: Colon and Rectum 2.0090, 15.0056, 17.0166
- Gastrointestinal Tumors: Esophagus 2.0010, 2.0012, 2.0013, 2.0014, 17.0166
- Gastrointestinal Tumors: Pancreas 2.0044, 17.0166
- Gastrointestinal Tumors: Stomach 2.0032
- Gastrointestinal Tumors: general 15.0056
- Genitourinary Tumors: Bladder 3.0007, 3.0024, 17.0166
- Genitourinary Tumors: Kidney 11.0001
- Gynecologic Tumors: Cervix 4.0017, 4.0021, 4.0084
- Gynecologic Tumors: Ovary 17.0066
- Gynecologic Tumors: Vulva 4.0084
- Head and Neck Tumors 12.0035, 12.0039, 12.0041, 12.0045, 17.0155, 17.0166
- Leukemia: Acute Leukemia (general) 6.0102
- Leukemia: Acute Lymphocytic Leukemia 6.0025, 6.0029, 6.0030, 6.0102, 6.0103, 15.0043, 17.0080
- Leukemia: Chronic Lymphocytic Leukemia 15.0074
- Leukemia: Chronic Nonlymphocytic Leukemia 6.0075
- Lung Tumors: Oat Cell 7.0016, 7.0017, 7.0024, 7.0027, 7.0032, 7.0080, 17.0091
- Lung Tumors: general 14.0007, 17.0166
- Lung Tumors: Non-Oat Cell 7.0074, 7.0080, 17.0094
- Lymphoma: Hodgkin's Disease 8.0016, 8.0017
- Lymphoma: Lymphosarcoma 15.0043, 17.0122
- Lymphoma: Reticulum Cell Sarcoma 15.0043, 17.0122
- Lymphoma: other 8.0038, 8.0045, 8.0056, 8.0057, 15.0074
- Lymphoma: general 8.0035, 17.0119
- Mesothelioma 10.0020
- Pediatric Solid Tumors: Ewing's Sarcoma 11.0014, 11.0015, 11.0016, 11.0018
- Pediatric Solid Tumors: Rhabdomyosarcoma 10.0025, 11.0010
- Pediatric Solid Tumors: Wilms' Embryoma 11.0001
- Pediatric Solid Tumors: general 15.0061
- Sarcoma: Osteogenic Sarcoma 17.0137, 17.0166
- Sarcoma: Soft Tissue Sarcoma 10.0020, 10.0021, 10.0022, 10.0023, 10.0024, 10.0025, 17.0166
- Skin Tumors: Melanoma 9.0022, 9.0029, 9.0041, 14.0007, 17.0166
- Solid Tumors: general 14.0006, 14.0007

Radiation: Mixed High/Low LET
- Brain and other CNS Tumors 13.0012
- Gastrointestinal Tumors: Esophagus 2.0004
- Gastrointestinal Tumors: Pancreas 2.0044
- Genitourinary Tumors: Bladder 3.0004
- Genitourinary Tumors: Prostate 3.0053
- Head and Neck Tumors 12.0008
- Lung Tumors: Non-Oat Cell 7.0044

Retinoids
- Breast Cancer 15.0051
- Genitourinary Tumors: Testis 15.0051
- Gynecologic Tumors: Ovary 15.0051
- Skin Tumors: Melanoma 15.0051

Rubidazone
- Leukemia: Acute Leukemia (general) 6.0080, 6.0081, 6.0093
- Leukemia: Acute Lymphocytic Leukemia 6.0093
- Leukemia: Acute Nonlymphocytic Leukemia 6.0045, 6.0046, 17.0081
- Pediatric Solid Tumors: general 11.0022
- Polycythemia Vera 6.0069

Spirogermanium
- Breast Cancer 1.0002
- Gastrointestinal Tumors: Colon and Rectum 2.0064
- Lymphoma: general 8.0053

Stanozolol
- Leukemia: Acute Nonlymphocytic Leukemia 6.0053

Stilphostrol
- Genitourinary Tumors: Prostate 3.0052

Streptonigrin
- Breast Cancer 17.0024
- Gastrointestinal Tumors: Colon and Rectum 17.0045
- Skin Tumors: Melanoma 17.0133

Streptozotocin
- Carcinoid 2.0052, 15.0017, 15.0026
- Endocrine Tumors: Endocrine Pancreas 2.0048, 15.0026
- Gastrointestinal Tumors: Colon and Rectum 2.0084, 2.0097
- Gastrointestinal Tumors: Gall Bladder 2.0128
- Gastrointestinal Tumors: Liver 2.0060, 2.0128

- Gastrointestinal Tumors: Pancreas 2.0039, 2.0040, 2.0041, 2.0048, 2.0049, 2.0052, 2.0128, 17.0029
- Gastrointestinal Tumors: general 15.0017
- Lymphoma: Hodgkin's Disease 8.0004, 8.0005, 8.0012, 15.0026
- Lymphoma: general 15.0026

Surgery

- Body Sites/Tumor Types: general 15.0060
- Brain and other CNS Tumors 13.0017, 13.0037, 13.0038
- Breast Cancer 1.0001, 1.0015, 1.0016, 1.0027, 1.0036, 1.0040, 1.0053, 1.0054, 1.0066, 1.0067, 1.0071, 1.0093, 1.0099, 1.0100, 1.0101, 1.0104, 17.0003
- Gastrointestinal Tumors: Colon and Rectum 2.0073, 2.0098, 2.0100, 2.0115, 2.0117, 2.0120, 2.0131, 2.0132, 2.0134, 17.0046
- Gastrointestinal Tumors: Esophagus 2.0007, 2.0014, 2.0015, 2.0132
- Gastrointestinal Tumors: Liver 2.0134
- Gastrointestinal Tumors: Pancreas 2.0131, 2.0134
- Gastrointestinal Tumors: Stomach 2.0019, 2.0032, 2.0036, 2.0131, 2.0132, 2.0134, 17.0028
- Gastrointestinal Tumors: general 2.0131
- Genitourinary Tumors: Bladder 3.0001, 3.0003, 3.0004, 3.0005, 3.0007, 3.0015, 3.0017, 3.0019, 3.0020, 3.0021, 3.0022, 3.0086
- Genitourinary Tumors: Kidney 3.0029, 3.0035, 3.0038, 3.0086, 11.0001
- Genitourinary Tumors: Testis 3.0068, 3.0072, 3.0073, 3.0074, 3.0078, 3.0079
- Genitourinary Tumors: other 3.0086, 15.0070
- Gynecologic Tumors: Cervix 4.0003, 4.0004, 4.0021, 15.0070
- Gynecologic Tumors: Ovary 4.0025, 4.0028, 4.0034, 4.0035, 4.0039, 4.0041, 4.0049, 4.0051, 15.0002
- Gynecologic Tumors: Uterus 4.0061, 4.0064
- Gynecologic Tumors: Vagina 4.0079, 4.0080
- Gynecologic Tumors: Vulva 4.0079, 4.0080
- Head and Neck Tumors 12.0008, 12.0012, 12.0014, 12.0021, 12.0022, 12.0023, 12.0027, 12.0030, 12.0034, 12.0035, 12.0037, 12.0041, 12.0042, 12.0045, 12.0051, 15.0070, 17.0153, 17.0155, 17.0158
- Leukemia: Acute Nonlymphocytic Leukemia 6.0043, 17.0083
- Leukemia: Chronic Lymphocytic Leukemia 15.0074
- Leukemia: general 6.0098
- Lung Tumors: Oat Cell 7.0013
- Lung Tumors: Non-Oat Cell 7.0074, 7.0093, 7.0094, 7.0100, 7.0103
- Lymphoma: Lymphosarcoma 17.0122
- Lymphoma: Reticulum Cell Sarcoma 17.0122
- Lymphoma: other 8.0037, 8.0056, 15.0074
- Lymphoma: general 8.0043
- Pediatric Solid Tumors: Ewing's Sarcoma 11.0012, 11.0013, 11.0015, 11.0018
- Pediatric Solid Tumors: Neuroblastoma 11.0004, 11.0008, 11.0009, 13.0017
- Pediatric Solid Tumors: Rhabdomyosarcoma 10.0025, 11.0010, 11.0011, 17.0148
- Pediatric Solid Tumors: Wilms' Embryoma 11.0001
- Sarcoma: Osteogenic Sarcoma 10.0004, 10.0007, 10.0008, 11.0027
- Sarcoma: Soft Tissue Sarcoma 10.0021, 10.0022, 10.0024, 10.0025, 17.0148
- Skin Tumors: Melanoma 9.0032, 9.0044, 9.0052, 9.0057, 9.0062, 9.0068, 9.0071, 17.0129

Surgery: Ablative

- Breast Cancer 1.0010, 1.0014, 1.0016, 1.0034, 1.0035, 1.0044, 1.0069, 1.0097, 1.0102, 17.0003
- Genitourinary Tumors: Prostate 3.0049, 3.0061, 3.0064, 17.0058
- Genitourinary Tumors: Testis 3.0068, 3.0073, 3.0074

Tamoxifen

- Breast Cancer 1.0003, 1.0011, 1.0012, 1.0014, 1.0016, 1.0017, 1.0018, 1.0019, 1.0020, 1.0025, 1.0033, 1.0035, 1.0036, 1.0047, 1.0054, 1.0062, 1.0070, 1.0081, 1.0085, 1.0090, 1.0092, 1.0093, 1.0097, 1.0103, 1.0104, 1.0106, 17.0006
- Gastrointestinal Tumors: Colon and Rectum 2.0076
- Genitourinary Tumors: Kidney 3.0032
- Genitourinary Tumors: Prostate 3.0057, 3.0059, 17.0057, 17.0059
- Gynecologic Tumors: Uterus 4.0067, 17.0069
- Skin Tumors: Melanoma 9.0001, 9.0034, 17.0126

beta-TGdR

- Endocrine Tumors: Endocrine Pancreas 2.0048
- Gastrointestinal Tumors: Pancreas 2.0048
- Leukemia: Acute Nonlymphocytic Leukemia 6.0041

Thiazolidine carboxylic acid

- Head and Neck Tumors 15.0073
- Lung Tumors: Non-Oat Cell 15.0073

Thio-TEPA

- Brain and other CNS Tumors 14.0006, 14.0007
- Breast Cancer 1.0004, 1.0068, 14.0006, 14.0007, 15.0045, 17.0015, 17.0024
- Gastrointestinal Tumors: Colon and Rectum 17.0045
- Genitourinary Tumors: Bladder 3.0014, 3.0020
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NCI-POB-7702 .... 6.0007
NCI-POB-7704 .... 8.0037
NCI-POB-7705 .... 11.0015
NCI-POB-7706 .... 11.0014
NCI-POB-7802 .... 17.0138
NCI-POB-7803 .... 11.0026
NCI-POB-7806 .... 8.0057
NCI-POB-7809 .... 11.0025
NCI-POB-7901 .... 15.0054
NCI-POB-7903 .... 17.0078
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NCI-SB-S6 .... 10.0023
NCI-SB-S7 .... 10.0024
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SWOG-7811 13.0015
SWOG-7812 13.0016
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DRUG SYNONYM AND ACRONYM APPENDIX

Drug Name and Synonym	Acronym	NSC Number
AAFC; Fluorocitabine	AAFC	166641
Acetaminophen; Tylenol		3991
Acetic Acid Hydrazide		2271
Acivicin *—see* AT-125		
Aclacinomycin		208734
Acronine; Acronycine		403169
ACTH; Adenocorticotropin; Corticotropin	ACTH	25933
Actidione *—see* Cycloheximide		
Actinomycin-D; Cosmegen; Dactinomycin	ACT-D, AD, DACT	3053
AD-32	AD-32	246131
ADAH *—see* CL-216942		
Adriamycin (HCl); Doxorubidin (HCl); Doxorubicin	ADR, ADM	123127
Adriamycin—DNA Complex	ADR-DNA	169534
Alanine Mustard		17663
L-Alanosine		153353
Aldactone; Aldalactone *—see* Spironolactone		
Alkeran *—see* Melphalan		
Allopurinol; Zyloprim		1390
Amethopterin *—see* Methotrexate		
Aminoglutethimide; Elipten; Cytadren	AGT, AG	No NSC
Aminopterin	APGA	739
2-Aminothiadiazole; Thiadiazole	ATDA	4728
Amphotericin-B		527017
m-AMSA; Methanesulfonamide derivative; Acridinyl anisidide	AMSA	249992
D-Amygdalin		15780
D,L-Amygdalin		251222
Anguidine	ANG	141537
Aniline Mustard		18429
p-Anisaldehyde, thiosemicarbazone		712
Anthracenedione *—see* Dihydroxyanthracenedione		
ARA-A *—see* Vidarabine phosphate		
Arabinosyl Cytosine *—see* Cytosine arabinoside		
ARA-C *—see* Cytosine arabinoside		
Aracytidine *—see* Cytosine arabinoside		
Asaley		167780
Ascorbic Acid; Vitamin C	VIT-C	33832
L-Asparaginase (E. carotovora)	L-ASP	106977
L-Asparaginase (E. coli)	L-ASP	109229
Aspirin		27223
AT-125; Acivicin	AT-125	163501
5-Azacytidine	AZC, 5- AZCR, 5- AZA	102816
8-Azaguanine; Guanozolo; Pathocidin	AZG	749
Azapicyl		68626
Azaribine; Azauridine triacetate; Triazure	AZR	67239
Azaserine; L-azaserine	AZS	742
Azathioprine	ATP	39084
6-Azauracil	AZU, 6-AZ	3425
6-Azauridine	AZUR	32074
Azauridine triacetate *—see* Azaribine		
Aziridinylbenzoquinone	AZQ	182986
Azotomycin; Diazomycin B; Duozomycin B		56654
Baker's Antifol; Triazinate	TZT, BAF	139105
BCG-Cell Wall Skeleton	BCG-CWS	No NSC
BCG-Connaught	BCG	B116341
BCG-F-70	BCG	No NSC
BCG-Glaxo	BCG	No NSC
BCG-MER *—see* MER-BCG		
BCG-Pasteur	BCG	B116328
BCG-Tice	BCG	B116327
BCNU; Carmustine	BCNU	409962
Benadryl		33299
Blenoxane *—see* Bleomycin		
Bleomycin; Blenoxane	BLEO, BLM	125066
5-Bromo-2'-deoxyuridine *—see* Broxuridine		
Broxuridine; 5-Bromo-2'-deoxyuridine	BUDR	38297
Bruceantin	BRU	165563
Bruneomycin *—see* Streptonigrin		
Busulfan; Myleran	BU	750
Calcium leukovorin *—see* Citrovorum Factor		
Calusterone	CLS	88536
Camptothecin		100880
Candida albicans		B116324
Carbestrol		19962
Carminomycin; Carubicin	CMM	180024
Carmustine *—see* BCNU		
Carubicin *—see* Carminomycin		
CCNU; Lomustine	CCNU	79037
Chlorambucil; Leukeran	CLB, CBL	3088
Chlorozotocin; DCNU	CLZ, DCNU	178248

DRUG SYNONYM AND ACRONYM APPENDIX

Drug Name and Synonym	Acronym	NSC Number
Chromomycin; Chromomycin A-3; Toyomycin		58514
Cimetidine		No NSC
Cisclomiphene (citrate); Clomiphene; Enclomiphene		151466
Cisplatin —*see* cis-Platinum		
Citrovorum Factor; Calcium Leukovorin; Leukovorin Calcium; Folinic Acid	CF, CFR, LV	3590
Clomiphene —*see* Cisclomiphene		
CL-216,942	ADC, ADAH	No NSC
Coenzyme Q	CoQ	140865
Colcemid(e) —*see* Demecolcine		
Colchamine —*see* Demecolcine		
Colchicine		757
Coparvax —*see* Corynebacterium parvum, B.W.		
Corticosterone		9705
Corticotropin —*see* ACTH		
Cortisol —*see* Hydrocortisone		
Cortisone		9703
Corynebacterium parvum, Burroughs-Wellcome; Coparvax	C. parvum, B.W.	220537
Corynebacterium parvum, Merieux	C. parvum, M.	197213
Cosmegen —*see* Actinomycin-D		
Crasnitin —*see* Asparaginase		
Cyclocytidine (hydrochloride)	CYC	145668
Cycloheximide; Actidione	TZA	185
Cycloleucine; 1-aminocyclopentane	CYL, ACP, CL	1026
Cyclophosphamide; Cytoxan; Endoxan	CTX, CPM, CYT, CYC	26271
Cyproterone acetate		81430
Cytarabine —*see* Cytosine arabinoside		
Cytembena		104801
Cytosar —*see* Cytosine arabinoside		
Cytosine arabinoside; Aracytidine; Arabinosyl Cytosine; Cytarabine; Cytosar	ARA-C	63878
Cytoxan —*see* Cyclophosphamide		
Dacarbazine —*see* DTIC		
Dactinomycin (-D) —*see* Actinomycin-D		
Daraprim —*see* Pyrimethamine		
Daunomycin; Rubidomycin; Daunorubicin	DNM, DNR, DRB	82151
Daunomycin-DNA Complex		169533
Daunorubicin —*see* Daunomycin		
DAVA —*see* Vindesine		
DCNU —*see* Chlorozotocin		
o,p'-DDD —*see* Mitotane		
DDMP; Metoprine	DDMP	19494
3-Deazauridine		126849
Decadron —*see* Dexamethasone		
Dehydroemetine		131546
Deltasone —*see* Prednisone		
Demecolcine; Colcemid; Colchamine		3096
2'-Deoxycoformycin; Pentostatin	DCF	218321
Deoxypyridoxine (hydrochloride)		3063
Depo-Provera —*see* Medroxyprogesterone acetate		
DES —*see* Diethylstilbestrol		
Dexamethasone; Decadron	DM, DXM, DSM	34521
D-Galactitol	DGTL	127939
DHEA Mustard		121210
cis-Diamminedichloroplatinum —*see* cis-Platinum		
Dianhydrodulcitol —*see* Dianhydrogalactitol		
Dianhydrogalactitol; Dianhydrodulcitol	DAG	132313
Diazomycin B —*see* Azotomycin		
6-Diazo-5-oxo-L-norleucine	DON	7365
Dibromodulcitol	DBD	104800
Dibromomannitol; Myelobromol	DBM	94100
Dichloroallyl lawsone		126771
Dichloromethotrexate	DCM	29630
Diethylstilbestrol; Stilbestrol; Stilboestrol	DES	3070
Diethylstilbestrol diphosphoric acid ester —*see* Stilphostrol		
Diglycoaldehyde; Inosine dialdehyde	INOX	118994
Dihydroxyanthracenedione-HCl; Anthracenedione; Mitoxantrone-HCl	DHAD	301739
Dimethylsulfoxide	DMSO	763
2,4-Dinitrochlorobenzene	DNCB	6292
Dinitrofluorobenzene	DNFB	33519
Dipyridamole; Persantine		515776
Doxorubicin —*see* Adriamycin		
Doxorubidin (hydrochloride) —*see* Adriamycin		
Drolban —*see* Dromostanolone propionate		
Dromostanolone; Drostanolone	DSP	26198
Dromostanolone propionate; Drolban		12198
Drostanolone —*see* Dromostanolone		

DRUG SYNONYM AND ACRONYM APPENDIX

Drug Name and Synonym	Acronym	NSC Number
DTIC; Dacarbazine	DTIC, DIC, ICDT	45388
Duborimycin	DBM	180510
Duozomycin B —*see* Azotomycin		
Eldisine —*see* Vindesine		
Ellipticine		71795
Emetine (hydrochloride)		33669
Enclomiphene (citrate) —*see* Cisclomiphene		
Endoxan —*see* Cyclophosphamide		
4-Epi-adriamycin-chlordate —*see* IMI-28		
Epipodophyllotoxin derivative —*see* VM-26		
Epipodophyllotoxin derivative —*see* VP-16213		
Epistiostanol —*see* Shionogi		
Epodyl; Ethoglucid		80439
Estracyt; Estramustine phosphate		89199
alpha-Estradiol		20293
beta-Estradiol		9895
Estradiol Mustard		112259
Estramustine		89201
Estramustine phosphate —*see* Estracyt		
Estriol		12169
Ethanol		85228
Ethidium chloride		84423
Ethinyl Estradiol		10973
Ethoglucid —*see* Epodyl		
Ethyl Hydrazide		No NSC
Etiocholanolone		50908
Etrenol —*see* Hycanthone mesylate		
Fenesterin —*see* Phenestrin		
Flagyl —*see* Metronidazole		
Florinef (acetate); Fluorocortisone		15186
Floxuridine; 5-Fluorodeoxyuridine	5-FUDR	27640
Fludrocortisone		11318
Fluorocitabine —*see* AAFC		
Fluorocortisone (acetate) —*see* Florinef (acetate)		
5-Fluorodeoxyuridine —*see* Floxuridine		
Fluorodopan; Ftordopan		73754
5-Fluorouracil	5-FU	19893
5-Fluorouridine		146604
Fluoxymesterone; Halotestin; Fluoxymestosterone	FXM	12165
Fluoxymestosterone —*see* Fluoxymesterone		
Folic Acid	FA	3073
Folinic Acid —*see* Citrovorum Factor		
Fosfestrol —*see* Stilphostrol		
Freund's Complete Adjuvant	FCA	No NSC
Ftorafur; Futraful	FT	148958
Ftordopan —*see* Fluorodopan		
Furosemide		269420
Futraful —*see* Ftorafur		
Galactitol	GTL	1944
D-Galactitol	DGTL	127939
Gallium nitrate	GAN	15200
Guanazole		1895
Guanazolo —*see* Azaguanine		
Hadacidin		521778
Halotestin —*see* Fluoxymesterone		
Hexamethylmelamine	HMM, HSA	13875
Hexestrol; Sinestrol		9894
Hycanthone		134434
Hycanthone mesylate; Etrenol		142982
Hydrea —*see* Hydroxyurea		
Hydrocortisone; Cortisol; 17-hydroxycorticosterone	HC	10483
Hydrocortisone sodium succinate	HDC	9152
17-Hydroxycorticosterone —*see* Hydrocortisone		
Hydroxyurea; Hydrea	HU	32065
ICRF-159; Razoxane	ICRF-159	129943
ICRF-187	ICRF-187	169780
Idoxuridine	5-IUDR	39661
Ifosfamide; Iphosphamide; Isophosphamide	IPP	109724
IMI-28 (4-Epi-adriamycin-chlordate)	IMI	256942
Imidazole-4-carboxamide dimethyltriazene —*see* DTIC		
Imidazole mustard —*see* TIC-mustard		
Indicine-N-oxide	INDI	132319
Inosine dialdehyde —*see* Diglycoaldehyde		
Interferon, mouse		305504
Iphosphamide —*see* Ifosfamide		
Isohexestrol		35752
Isoniazid	INH	9659
Isophosphamide —*see* Ifosfamide		
Lapachol		11905
LEO-1031 —*see* Prednimustine		
Leukeran —*see* Chlorambucil		
Leukerin —*see* 6-Mercaptopurine		

DRUG SYNONYM AND ACRONYM APPENDIX

Drug Name and Synonym	Acronym	NSC Number
Leukovorin Calcium —*see* Citrovorum Factor		
Leurocristine —*see* Vincristine (sulfate)		
Levamisole; Tetramisole; Levasole; Tramisol	LEV	177023
Levasole —*see* Levamisole		
Lithium carbonate		16895
Lomustine —*see* CCNU		
Mannitol		9256
Matulane —*see* Procarbazine		
Maytansine	MTS	153858
Mechlorethamine hydrochloride —*see* Nitrogen Mustard		
Medrogestone	MG	123018
Medrol —*see* Methylprednisolone		
Medroxyprogesterone acetate; Depo-Provera; Provera	MPA, MAP	26386
Megace —*see* Megestrol acetate		
Megestrol acetate; Megace	MEG	71423
Melphalan; L-phenylalanine mustard; Alkeran	L-PAM	8806
MER-BCG	MER	143769
6-Mercaptopurine; Leukerin; Purinethol	6-MP	755
6-Mercaptopurine riboside	6-MP-R	4911
Mestranol		84032
Methanesulfonamide derivative —*see* m-AMSA		
Methotrexate; Amethopterin	MTX	740
Methyl-CCNU; Semustine	MeCCNU	95441
Methyl-GAG	MeGAG, MGGH, MGBG	32946
Methylprednisolone; Medrol	MePRDL	19987
Methyltrienolone; Metribolone		92858
Meticorten —*see* Prednisone		
Metoprine —*see* DDMP		
Metribolone —*see* Methyltrienolone		
Metronidazole; Flagyl		69587
Misonidazole; Ro-07-0582	MNI	261037
Mithracin —*see* Mithramycin		
Mithramycin; Mithracin		24559
Mitomycin-C; Mutacin	MITO, MITO-C	26980
Mitotane; o,p'-DDD		38721
Mitoxantrone-Hcl —*see* Dihydroxyanthracenedione		
Mitoxine —*see* Nitrogen Mustard		
Mustargen —*see* Nitrogen Mustard		

Drug Name and Synonym	Acronym	NSC Number
Mutacin —*see* Mitomycin-C		
Myelobromol —*see* Dibromomannitol		
Myleran —*see* Busulfan		
Nafoxidine (hydrochloride)	NFX	70735
Nandrolone; 19-Nortestosterone		3351
Natulan —*see* Procarbazine (hydrochloride)		
Neocarzinostatin	NZS, NCS	157365
Nitrogen Mustard; Mitoxine; Mustargen; Mechlorethamine hydrochloride	NM, HN-2	762
Nolvadex —*see* Tamoxifen (citrate)		
Norethisterone acetate		22844
Norethynodrel		15432
Norgamem —*see* L-4 Thiazolidine carboxylic acid		
19-Nortestosterone —*see* Nandrolone		
OK-432; Picibanil		293562
Oncovin —*see* Vincristine (sulfate)		
Oxymetholone		No NSC
PALA; N-(phosphonoacetyl)-L-aspartate	PALA	224131
Papaverine		136630
Papaverine hydrochloride		35443
Pathocidin —*see* 8-Azaguanine		
PCNU		95466
Pentamethylmelamine		118742
Peptichemio		247516
Persantine —*see* Dipyridamole		
Phenestrin; Fenesterin		104469
Phenetharbital —*see* Phetharbitol		
L-Phenylalanine mustard —*see* Melphalan		
Phetharbitol; Phenetharbital		85043
Phosphorus-32; Radiophosphorous	P-32	No NSC
Picibanil —*see* OK-432		
2,5-Piperazinedione	PZD	135758
cis-Platinum; Cisplatin; cis-Diamminedichloroplatinum	CACP, DDP, CPDD, CDDP	119875
Podophyllic Acid (Na salt)		35475
Poly-AU (Polyadenylic-polyuracilic Acid)		120951
Poly-IC (Polyriboinosinic-polyribocytidilic Acid)		120949
Porfiromycin		56410
PPD of Tuberculin		B116326
Prednimustine; LEO-1031		134087
Prednisolone	PRDL	9900
Prednisolone succinate		9151
Prednisone; Deltasone; Meticorten	PRED, PDN, PRD	10023

DRUG SYNONYM AND ACRONYM APPENDIX

Drug Name and Synonym	Acronym	NSC Number
Procarbazine (hydrochloride); Matulane; Natulan; Methyl hydrazine derivative	PCB, MIH	77213
Progesterone		9704
Provera —*see* Medroxyprogesterone acetate		
Pseudoisocytidine		279852
Purinethol —*see* 6-Mercaptopurine		
Pyran copolymer		46015
Pyrazofurin; Pyrazomycin	PRZF	143095
Pyrazomycin —*see* Pyrazofurin		
Pyridoxine (hydrochloride); Vitamin B6	VIT-B6	36225
Pyrimethamine; Daraprim		3061
Radiophosphorus —*see* Phosphorus-32		
Razoxane —*see* ICRF-159		
13-cis-Retinoic acid		No NSC
Ribavirin —*see* Virazole		
Rifamycin (SV)		133100
Ro-07-0582 —*see* Misonidazole		
Rubidazone (hydrochloride)	RBD, RUB	164011
Rubidomycin —*see* Daunomycin		
Semustine —*see* Methyl CCNU		
Shionogi; Epistiostanol		194684
Sinestrol —*see* Hexestrol		
Sodium butyrate		174280
Sodium fluoride		77385
Sparsomycin A —*see* Tubercidin		
Spirogermanium	SPG	192965
Spironolactone; Aldalactone; Aldactone	SPL	150399
Stanozolol; Winstrol		43193
Stilbestrol —*see* Diethylstilbestrol		
Stilboestrol —*see* Diethylstilbestrol		
Stilphostrol; Fosfestrol; Diethylstilbestrol, diphosphoric acid ester		10481
Streptonigrin; Bruneomycin	STN, STP	45383
Streptozotocin; Zanosar	SZC, STP, STZ	85998
Tamoxifen (citrate); Nolvadex	TMX	180973
Teslac —*see* Testolactone		
Testolactone; Teslac	TL	23759
Testolactone derivative		76164
Testololactone	TLL	12173
Testosterone		9700
Testosterone enenthate		17591
Testosterone propionate		9166
d-Tetrandine		77037
Tetrahydrouridine	THU	112907
Tetramisole —*see* Levamisole		
alpha-TGdR (alpha-2'-Deoxythioguanosine)	a-TGdR	71851
beta-TGdR (beta-2'-Deoxythioguanosine)	b-TGdR, BTGdR	71261
Thaliblastine —*see* Thalicarpine		
Thalicarpine; Thaliblastine	TC	68075
Thiabendazole	TBZ	81948
Thiadiazole —*see* 2-Aminothiadiazole		
L-4 Thiazolidine carboxylic acid; Norgamem		25855
6-Thioguanine	TTG, TG, 6-TG, 6-THIO	752
Thioguanosine	TGR	29422
alpha-Thioguanosine deoxyriboside —*see* alpha-TGdR		
beta-Thioguanosine deoxyriboside —*see* beta-TGdR		
Thiotepa; Thio-tepa		6396
Thymidine	TDR, TdR	21548
Thymosin		No NSC
TIC-mustard; Imidazole mustard; TIC-HN2	BIC, BTIC	82196
Tilorone (hydrochloride)		143969
TMCA (Trimethylcolchicinic Acid)	TMCA	36354
Toyomycin —*see* Chromomycin		
Tramisol —*see* Levamisole		
Tretamine —*see* Triethylenemelamine		
Triazinate —*see* Baker's Antifol		
Triazure —*see* Azaribine		
Triethylenemelamine; Tetramine	TEM	9706
Trifluorothymidine —*see* Trifluridine		
Trifluridine; Trifluorothymidine	F3TDR	75520
L-Triiodothyronine	TRI-I	80774
Trimethoprim		106568
Trimethylcolchicinic Acid —*see* TMCA		
Trofosfamide; Trosfosfamid	TFF, TC	109723
Trosfosfamid —*see* Trofosfamide		
Tubercidin; Sparsomycin A	TBC	56408
Tylenol —*see* Acetaminophen		
Velban —*see* Vinblastine (sulfate)		
Vidarabine phosphate	ARA-A	247519
Vinblastine (sulfate); Velban; Vincaleukoblastine	VBL, VLB	49842

DRUG SYNONYM AND ACRONYM APPENDIX

Drug Name and Synonym	Acronym	NSC Number
Vincaleukoblastine derivative —*see* Vindesine (sulfate)		
Vincaleukoblastine sulfate —*see* Vinblastine (sulfate)		
Vincristine (sulfate); Oncovin; Leurocristine	VCR, LCR	67574
Vindesine (sulfate); DAVA; Eldisine; Vincaleukoblastine derivative	DAVA, DVA	245467
Virazole; Ribavirin		163039
Vitamin A	VIT-A	122759
Vitamin B6 —*see* Pyridoxine (hydrochloride)		
Vitamin C —*see* Ascorbic Acid		
Vitamin D	VIT-D	62792
Vitamin E	VIT-E	82623
VM-26; Epipodophyllotoxin derivative	VM-26, PTG	122819
VP-16213; Epipodophyllotoxin derivative	VP-16	141540
Warfarin; Coumadin; Athrombin-K		59813
Winstrol —*see* Stanozolol		
WR-2721		296961
Yoshi-864; Dimethanesulfonate ester derivative	Yoshi	102627
Zanosar —*see* Streptozotocin		

PROTOCOL IDENTIFICATION NUMBER ABBREVIATION APPENDIX

ACC—Aichi Cancer Center (Nagoya, Japan)
ACSCS—American Cancer Society Collaborative Study
ADENO—adenocarcinoma
AIL—Association Against Leukemia Study Group (Italy)
AIO—Association of Interdisciplinary Oncology of the German Cancer Society
AL—acute leukemia
ALB—*see* CLB
ALL—acute lymphocytic leukemia
AML—acute myelogenous leukemia
ANLL—acute nonlymphocytic leukemia
ANSG—Australian Neuroblastoma Study Group
ARG—Argentina
AUS—Australia
AUT—Austria
AZL—Academisch Ziekenhuis Leiden (The Netherlands)

BCRP—Baltimore Cancer Research Program
BCTF—Breast Cancer Task Force
BL—bladder
BLCGL—blast crisis, chronic granulocytic leukemia
BLG—Belgium
BMT—bone marrow transplantation
BN—brain
BOL—Bologna
BR—breast
BR—bronchogenic carcinoma
BRA—Brazil
BRE—breast
BS—Basel, Switzerland
BTRC—Brain Tumor Research Center (San Francisco)
BTSG—Brain Tumor Study Group

CA—California
CAN—Canada
CAR—Cardiff, Wales
CBCG—Cooperative Breast Cancer Group
CCG—Children's Cancer Study Group
CCGAL—Cancer Chemotherapy Center-Acute Leukemia (Japan)
CCH—Charing Cross Hospital (London)
CCI—Cross Cancer Institute (Canada)
CCSF—Comprehensive Cancer Center for the State of Florida
CCWA—Cancer Council of Western Australia
CE—cerebral malignancies
CFB—Centre Francois Baclesse (Caen, France)
CHILE—Chile
CHMC—City of Hope Medical Center (Duarte, California)
CHOC—Children's Hospital Oncology Center (Denver)
CHOP—Children's Hospital of Philadelphia
CLB—Cancer and Leukemia Cooperative Group B (formerly ALB)
CLL—chronic lymphocytic leukemia
CMH—Central Military Hospital (Argentina)
CML—chronic myelocytic leukemia
CNS—central nervous system
COG—Central Oncology Group
COHMC—Children's Orthopedic Hospital and Medical Center (Seattle)
COL—Colombia
COSTARICA—Costa Rica
CPB—Clinical Pharmacology Branch, NCI
CPB—primary bronchial carcinoma
CRC—colorectal carcinoma
CWS—cell wall skeleton
CZE—Czechoslovakia

DAN—Denmark
DATECA—Danish Testicular Carcinoma Project
DD—disseminated disease
DMA—Dept. of Medicine A, Roswell Park Memorial Inst.
DT—Developmental Therapeutics (MDA)
DUT—The Netherlands

ECOG—*see* EST
EORTC—European Organization for Research on Treatment of Cancer
EPI—epidermoid carcinoma
ESO—esophageal
EST—Eastern Cooperative Oncology Group (formerly ECOG)
EU—Emory University (Atlanta)
EUR—Europe
EWI—Ewing's sarcoma
EWING—Ewing's sarcoma

FCLC—Federation des Centres de Lutte Contre le Cancer (France)
FG—Fondation Bergonie (Bordeaux, France)
FRE—France

GA—Georgia
GATLA—Grupo Argentino de Tratamiento de la Leucemia Aguda
GCT—germ cell tumor
GER—Germany
GH—Geneva Hospital (Switzerland)
GI—gastrointestinal
GIC—colon carcinoma
GOG—Gynecologic Oncology Group
GTSG—Gastrointestinal Tumor Study Group
GU—genitourinary
GUMO—Georgetown University Hospital, Division of Medical Oncology (Washington, D.C.)
GUY—Guy's Hospital (London)

HD—Hodgkin's Disease
HH—Hammersmith Hospital (London)
HIC—Human Investigation Committee, Yale University
HN—head and neck
HNCP—Head and Neck Contracts Program
HR—Hospital de Radiationes (Buenos Aires)

IB—Immunology Branch, NCI

PROTOCOL IDENTIFICATION NUMBER ABBREVIATION APPENDIX

IGM—International Group for the Clinical Study of Melanoma
IGR—Institut Gustave-Roussy (Villejuif, France)
IL—Illinois
INA—India
INEN—Instituto Nacional de Enfermedades Neoplasicas (Lima)
IOL—Institute of Oncology (Ljubljana)
IRE—Ireland
IRS—Intergroup Rhabdomyosarcoma Study
ISR—Israel
ITA—Italy
ITM—Istituto Nazionale Tumori (Milan)
JAP—Japan
JHOC—Johns Hopkins Oncology Center
JRD—Janssen R&D, Inc.
KCH—King's College Hospital (London)
KLSG—Kanto Leukemia Study Group (Japan)
L—lung
LACRIP—Latin American Cancer Research Information Project
LAM—acute myelogenous leukemia
LBL—Lawrence Berkeley Laboratory
LC—lung cancer
LCS—Leukemia Group of Central Sweden (Stockholm)
LCSG—Lung Cancer Study Group
LEU—leukemia
LEVAM—Levamisole
LLA—lymphocytic leukemia
LLC—chronic lymphocytic leukemia
LMC—chronic myelogenous leukemia
LUN—lung
LY—lymphoma
LYM—lymphoma
M—metastatic
MA—Massachusetts
MAYO—Mayo Clinic
MB—Medicine Branch, NCI
MBCSG—Metastatic Breast Cancer Study Group (Canada)
MCW—Medical College of Wisconsin (Milwaukee)
MD—Maryland
MDA—M.D. Anderson Hospital and Tumor Institute
MDAR—MDA Office of Research
ME—melanoma
MEL—melanoma
MELANO—melanoma
MEX—Mexico
MI—Michigan
MIDWEST—Midwest Childhood Cancer Center (Milwaukee)
MIL—Milan
MM—multiple myeloma
MOB—Medical Oncology Branch, NCI
MRC—Medical Research Council (United Kingdom)
MSAR—melanoma and sarcoma
MSG—Melanoma Study Group (Canada)
MSHMC—Milton S. Hershey Medical Center (Pennsylvania)
MSKCC—Memorial Sloan Kettering Cancer Center (formerly SK)
MTS—Mount Sinai School of Medicine (New York City)
MY—multiple myeloma
MYEL—multiple myeloma
NB—neuroblastoma
NBCCGA—National Bladder Cancer Collaborative Group A
NBCG—Northern Breast Cancer Study Group (New Zealand)
NBCP—National Bladder Cancer Project
NC—North Carolina
NCCH—National Cancer Center Hospital (Tokyo)
NCCTG—North Central Cancer Therapy Group (Rochester, Minnesota)
NCI—National Cancer Institute
NCIC—National Cancer Institute of Canada
NCOG—Northern California Oncology Group
N-CWS—Nocardia rubra cell wall skeleton
NEURO—neuroblastoma
NHL—Non-Hodgkin's lymphoma
NHLSG—Non-Hodgkin's Lymphoma Study Group
NOR—Norway
NPC—nasopharyngeal cancer
NPCP—National Prostatic Cancer Project
NRH—Norwegian Radium Hospital (Oslo)
NSABP—National Surgical Adjuvant Breast Project (formerly PBCTG)
NUTR—nutrition
NWTS—National Wilms' Tumor Study Group
NY—New York
NZL—New Zealand
OCC—Ovarian Cancer Chemotherapy
OCF—Ontario Cancer Foundation
OCI—Ontario Cancer Institute
OCSG—Ovarian Cancer Study Group
OH—Ohio
OK—Oklahoma
OMRF—Oklahoma Medical Research Foundation
OS—osteosarcoma
OSAKO—Cooperative Oncology Group of Eastern Switzerland
OSITC—Organizacion Sudamericana de Investigacion en el Tratamiento del Cancer (Argentina)
OST—osteogenic sarcoma
OSU—Ohio State University
OV—ovary
OVCA—ovarian cancer
OVG—EORTC Ovarian Group
OXF—Oxford, England
P—Pilot Study
PA—Pennsylvania
PAN—pancreas
PANC—pancreas
PAR—Paris
PBCTG—Primary Breast Cancer Therapy Group (*see* NSABP)
PERU—Peru
PIPER—Piperazinedione
PL—pleuritis carcinomatosa
PMC—Peter MacCallum Clinic (Melbourne)
PNH—Portsmouth Naval Hospital
POA—Piedmont Oncology Association (Winston-Salem, NC)
POACSG—Postoperative Adjuvant Chemotherapy Study Group (Japan)
POB—Pediatric Oncology Branch, NCI
PODOPH—Podophyllum compounds

PROTOCOL IDENTIFICATION NUMBER ABBREVIATION APPENDIX

POL—Poland
PPC—Pharmacy/Pharmacology Committee, RPMI
PR—prostate
PROT—protocol
PT—polycythemia trial
PU—pulmonary
PVSG—Polycythemia Vera Study Group

R—recurrent
R—refractory
RCH—Royal Children's Hospital (Melbourne)
REN—renal carcinoma
RET—retinoblastoma
RHDG—Radiotherapy Hodgkin's Disease Group
RI—Royal Infirmary (Glasgow)
RMH—Royal Melbourne Hospital (Australia)
RMS—rhabdomyosarcoma
RNH—Rivadavia National Hospital (Buenos Aires)
ROB—Radiation Oncology Branch, NCI
RPMI—Roswell Park Memorial Institute
RRTI—Rotterdam Radiotherapy Institute (The Netherlands)
RTOG—Radiation Therapy Oncology Group
RUS—Russia

SAFR—South Africa
SAKK—Swiss Group for Clinical Cancer Research; Groupe Suisse de Recherche Clinique sur le Cancer; Schweizeriche Arbeitsgruppe fuer Klinische Krebsforschung und Strahlentherapeutische Kliniken von Basel, Bern, Genf, Lausanne, St. Gallen und Zurich
SAO—osteogenic sarcoma
SAR—sarcoma
SB—Surgery Branch, NCI
SC—stomach cancer
SCC—Southern California Cancer Center (Los Angeles)
SEG—Southeastern Cancer Study Group
SFCC—Sidney Farber Cancer Center (formerly SF)
SFCR—Stehlin Foundation for Cancer Research (Houston, TX)
SGBC—Study Group for Bronchogenic Carcinoma (Belgium)
SIOP—International Society for Pediatric Oncology
SJCRH—St. Jude Children's Research Hospital (Memphis)
SK—*see* MSKCC
SNC—central nervous system
ST—solid tumor
SVH—St. Vincent's Hospital and Medical Center (New York City)
SWE—Sweden
SWOG—Southwest Oncology Group
SWS—Switzerland

TAT—Tata Memorial Hospital (Bombay)
TC—testicular cancer
TCIS—Testicular Cancer Intergroup Study
TGH—Toronto General Hospital (Canada)
THY—thyroid
TN—Tennessee
TO—Toronto
TOT—total therapy
TSC—Tokai Stomach Cancer Immuno/Chemotherapy Cooperative Study Group (Nagoya, Japan)
TT—total therapy
TX—Texas

UARIZ—University of Arizona
UCLA—University of California at Los Angeles
UHW—University Hospital of Wales
UICC—Union Internationale Contre le Cancer
UK—United Kingdom
UKM—United Kingdom
UNCHIM—Unite de Chimiotherapie, Hopital St. Louis (Paris)
UORG—Uro-Oncology Research Group
URU—Uruguay
UTBG—University of Toronto Breast Group
UTENN—University of Tennessee
UTHSC—Univ. Texas Health Science Center (San Antonio)

VA—Veterans Administration
VA—Virginia
VALG—Veterans Administration Lung Cancer Study Group
VAMC—Veterans Administration Medical Center (Asheville, NC)
VASAG—Veterans Administration Surgical Adjuvant Cancer Chemotherapy Study Group
VASOG—Veterans Administration Surgical Oncology Group
VEN—Venezuela

WA—Washington
WCCC—Wisconsin Clinical Cancer Center
WCG—Western Cancer Study Group
WDP—WCG Pilot Study
WFU—Wake Forest University
WILMS—Wilms' Tumor
WLT—WCG Limited Center Trials
WPB—Working Party on Bleomycin
WPBS—Working Party on Bone Sarcoma
WPL—Working Party for Therapy of Lung Cancer
WSU—Wayne State University
WTSG—*see* NWTS

YALE—Yale University
YORK—Yorkshire Regional Chemotherapy Group
YRCO—Yorkshire Regional Cancer Organization
YUG—Yugoslavia

MEDICAL AND MEASUREMENT ABBREVIATION APPENDIX

AEL	acute erythroleukemia
AFIP	Armed Forces Institute of Pathology
AFP	alpha fetoprotein
AG ratio	albumin/globulin ratio
AHL	acute histiocytic leukemia
AJC	American Joint Committee
ALL	acute lymphocytic leukemia
AML	acute myelogenous leukemia
AMML	acute myelomonocytic leukemia
AMOL	acute monocytic leukemia (A Monol)
amu	atomic mass unit
ANA	antinucleic acid(s)
ANC	absolute neutrophil count(s)
ANLL	adult nonlymphocytic leukemia
APL	acute promyelocytic leukemia
ASL	acute stem-cell leukemia
AUL	acute undifferentiated leukemia
BAE	barium enema
BM, bm	bone marrow
BMT	bone marrow transplantation
BSO	bilateral salpingo-oophorectomy
BSP	bromsulphalein
BUN	blood urea nitrogen
CAT, CTT	computerized axial tomography
cbc	complete blood count
CDP	clinical disease present
CEA	carcinoembryonic antigen
CFU	colony-forming units
CGL	chronic granulocytic leukemia
Ci	curie
CLL	chronic lymphocytic leukemia
cm	centimeter(s)
CML	chronic myelogenous leukemia
CNS	Central Nervous System
CORE	cobalt-60 rad equivalent dose
CPK	creatine phosphokinase
CR	(patients with) complete response
CSF	cerebrospinal fluid
cu	cubic
d	day(s)
D and C	dilation and curettage
DHA	dehydroepiandrostone
DHR	delayed hypersensitivity reaction
DNA	deoxyribonucleic acid
DNCB	dinitrochlorobenzene
DP	(patients with) disease progression
EBP	estrogen binding protein
EBV	Epstein-Barr virus
ECG, EKG	electrocardiogram
EEG	electroencephalogram
EM	electron microscope
EMD	extramedullary disease
EMI	computerized axial tomography
ER	estrogen receptor(s)
ESR	erythrocyte sedimentation rate
FBS	fasting blood sugar
fmol	fentamoles
FSH	follicle-stimulating hormone
FVC	functional vital capacity
g	gram(s)
GI	gastrointestinal
G6PD	glucose-6-phosphate dehydrogenase
GU	genitourinary
Hb	hemoglobin
HBSA	hepatitis type-B surface antigen
HCG	human chorionic gonadotropin
HER	high-energy radiation
5-HIAA	5-hydroxyindoleacetic acid
HLA	histocompatibility antigens
HTB	high tumor burden
HVA	homovanillic acid
ia	intra-arterial
IBMR	impaired bone marrow reserve
ic	intracutaneous
id	intradermal
Ig	immunoglobulins
il	intralymphatic
im	intramuscular
ip	intraperitoneal
it	intrathecal
IU	International Units
iv	intravenous
IVP	intravenous pyelogram
kg	kilogram
KLH	keyhole limpet hemocyanin
KPS	Karnofsky performance status
KUB	kidney, ureter, bladder
LAI	leukocyte adherence inhibition
LDH	lactic dehydrogenase
LET	linear energy transfer
LFT	liver function test(s)
LH	luteinizing hormone
LL	lymphoma leukemia
LP	lumbar puncture
LTB	low tumor burden
M	molar
m	meter
MBV	mixed bacterial vaccine
mCi	millicurie(s)
mEq	milliequivalent
MER	methanol extraction residue of BCG
MEV, MeV	million electron volts
mg	milligram(s)
MHz	megahertz (microwaves)
min	minute(s)
ML	meningeal leukemia
ml	milliliter(s)
MLC	mixed lymphocyte culture
MLD	minimal lethal dose
mm	millimeters
N	normal concentration

MEDICAL AND MEASUREMENT ABBREVIATION APPENDIX

NC	(patients with) no change
NCD	(patients with) no clinical evidence of disease
NED	(patients with) no evidence of disease
ng	nanogram
NHL	non-Hodgkin's lymphoma
NPN	non-protein nitrogen
NPO	nothing by mouth
NR	(patients with) no response
NS	normal saline
PAS	periodic acid-Schiff
PBI	protein-bound iodine
pc	after meals (post cibus)
PD	(patients with) progressive disease
PE	protected environment
PEPA	protected environment with prophylactic antibiotics
PHA	phytohemaglutinin
Ph-1	Philadelphia chromosome
po	orally
PPD	purified protein derivative of tuberculin
ppm	parts per million
PR	(patients with) partial response
prn	as tolerated
PT	prothrombin time
PTT	partial thromboplastin time
PWM	pokeweed mitogen
q	every
R	roentgen
rad	radiation absorbed dose
rbc	red blood cells
RBE	relative biological effectiveness
rf	radiofrequency (current)
RIA	radioimmune assay
RNA	ribonucleic acid
rpm	revolutions per minute
sc	subcutaneous
SD	(patients with) stable disease
SGOT	serum glutamic-oxoacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
SMA	sequential multiple analyser
sqm	square meter
SSD	source—skin distance
STI	systolic intervals
SVC	superior vena cava
TAH	total abdominal hysterectomy
TBI	total body irradiation
TCV	tumor cell vaccine
tid	three times a day
TLC	thin-layer chromatography
TNM	Tumor-Node-Metastasis Clinical Staging System
TRH	thyrotropin-releasing hormones
TSH	thyrotropin
TUR	transurethral resection
U	unit(s)
UCG	urinary chorionic gonadotropins
UGI	upper GI series
UV	ultraviolet
VDRL	serologic test for syphilis
VMA	vanillyl mandalic acid
VMTCE	viral modified tumor cell membrane extract (viral oncolysate)
vs.	versus
wbc	white blood cells
wt	weight
x	times

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